Access DB# 71334

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jeffrey E. Russel Examiner #: 62785 (STIC) Date: 7-18-2002
Art Unit: 1653 Phone Number 30 8-3975 Serial Number: 09/783,248
Mail Box and Bldg/Room Location: CM1-9801 / CM1-9807 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Matrix Metalloprotelnase Inhibitors

Inventors (please provide full names): C. Decicco, D. Nelson, J. Barrett, A. Carpenter, J. Oven, M. Rajopadhye

Earliest Priority Filing Date: 2-14-2001

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search the circled portion of the attached structure, with the alkyl group having a variable length (C_1-C_{10} would be fine). If there are no hits, please search the cyclic parts of the circled portion (i.e., leave out the diaminoalkyl part). keywords are conjugat?, metalloprotease, cytotoxi?, cancer, retinopathy, tumor, ~~[illegible]~~macular degeneration.

Thank you.

JER

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STAFF USE ONLY

Searcher: Shaporia
Searcher Phone #: 308-4499
Searcher Location:
Date Searcher Picked Up:
Date Completed: 7/19/02
Searcher Prep & Review Time:
Clerical Prep Time:
Online Time:

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

PTO-1590 (8-01)

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FILE COVERS 1907 - 19 Jul 2002  VOL 137 ISS 4
FILE LAST UPDATED: 18 Jul 2002  (20020718/ED)

 This file contains CAS Registry Numbers for easy and accurate
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CAS roles have been modified effective December 16, 2001. Please
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information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

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L1                STR
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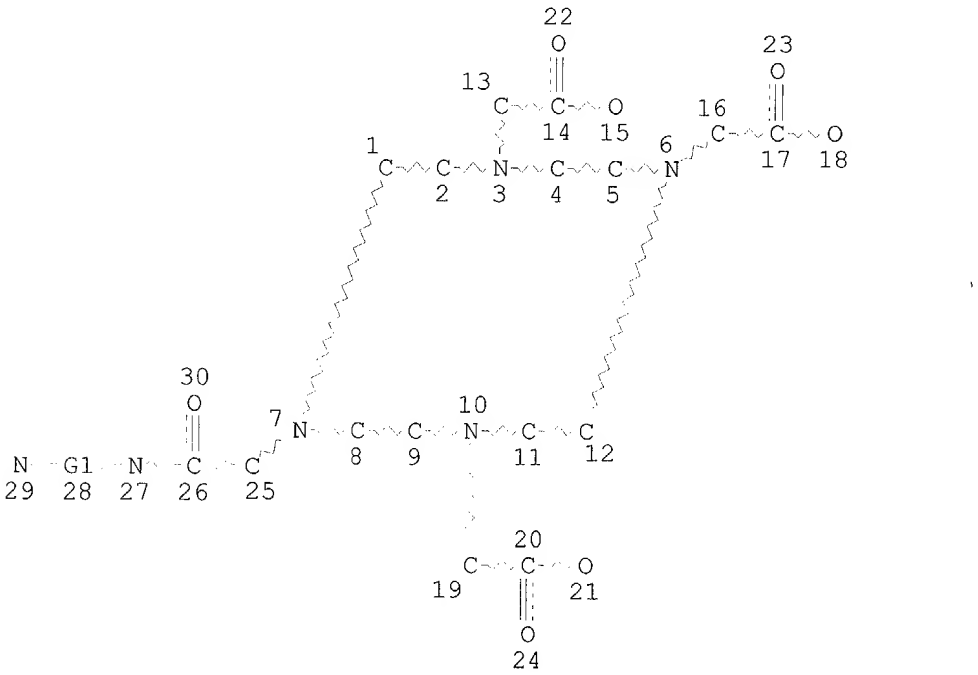

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REP G1=(1-10) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  30

STEREO ATTRIBUTES: NONE
L3          286 SEA FILE=REGISTRY SSS FUL L1
L4        27429 SEA FILE=REGISTRY ABB=ON  PLU=ON  CONJUGAT? OR METALLOPRO? OR
                CYTOTOXI?
L5           90 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3
L6       326269 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR ?CONJUGAT? OR ?METALLOPR
                O? OR ?CYTOTOXI?
L9           19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 (L)(?CANCER? OR ?TUMOR? OR
                ?NEOPLAS? OR ?MALIG? OR ?MACUL? OR ?DEGENER?)
L10          21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5(L)L6
L11          35 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR L10


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L11  ANSWER 1 OF 35  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:391572  HCAPLUS
DOCUMENT NUMBER:          136:406944
TITLE:                    Conjugates of antioxidants with metal chelating
                          ligands for use in diagnostic and therapeutic
                          applications
INVENTOR(S):              Ranganathan, Ramachandra S.; Fan, Helen; Tweedle,
                          Michael F.
PATENT ASSIGNEE(S):       Bracco International BV, Neth.
SOURCE:                   PCT Int. Appl., 71 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2002040060      A2   20020523       WO 2001-US46002  20011031
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
             UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    US 2000-244547P  P  20001031
OTHER SOURCE(S):          MARPAT 136:406944
AB   The invention provides radiopharmaceuticals for diagnostic and therapeutic
     applications, conjugates of antioxidants with metal chelating ligands,
     intermediate compds., methods of making such radiopharmaceuticals,
     ligands, and intermediate compds., and kits for prepg. the
     radiopharmaceutical complexes.
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IT **428817-75-8P 428817-76-9P 428817-77-0P**
428817-79-2P 428817-80-5P 428817-81-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of **conjugates** of antioxidants with metal chelating ligands for use in diagnostic and therapeutic applications)

L11 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:353971 HCAPLUS
DOCUMENT NUMBER: 136:365879
TITLE: Gastrin receptor-avid peptide conjugates and radionuclide complexes
INVENTOR(S): Hoffman, Timothy J.; Volkert, Wynn A.; Sieckman, Gary; Smith, Charles J.; Gali, Hariprasad
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 60 pp., Cont.-in-part of U.S. Ser. No. 537,423.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002054855	A1	20020509	US 2001-847134	20010502

PRIORITY APPLN. INFO.: US 2000-537423 A2 20000329
AB A compd. for use as a therapeutic or diagnostic radiopharmaceutical includes a group capable of complexing a medically useful metal attached to a moiety which is capable of binding to a gastrin releasing peptide receptor. A method for treating a subject having a neoplastic disease includes administering to the subject an effective amt. of a radiopharmaceutical having a metal chelated with a chelating group attached to a-moiety capable of binding to a gastrin releasing peptide receptor expressed on tumor cells with subsequent internalization inside of the cell. A method of forming a therapeutic or diagnostic compd. includes reacting a metal synthon with a chelating group covalently linked with a moiety capable of binding a gastrin releasing peptide receptor. Numerous examples are provided of the prepn., properties, gastrin releasing peptide receptor affinity, tumor uptake and biodistribution of DOTA radionuclide complexes conjugated to bombesin(7-14)NH2 via linkers such as 5-aminovaleric acid and 8-aminooctanoic acid.
IT **422512-72-9P 422512-75-2P 422512-78-5P**
422512-81-0P
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(gastrin receptor-avid peptide **conjugates** and radionuclide complexes: prepn., **tumor** uptake and biodistribution)

L11 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:267288 HCAPLUS
DOCUMENT NUMBER: 137:2480
TITLE: Neuroendocrine tumor targeting: study of novel gallium-labeled somatostatin radiopeptides in a rat pancreatic tumor model
AUTHOR(S): Froidevaux, Sylvie; Eberle, Alex N.; Christe, Martine; Sumanovski, Lazar; Heppeler, Axel; Schmiti, Jorg S.; Eisenwiener, Klaus; Beglinger, Christoph; Macke, Helmut R.

CORPORATE SOURCE: Department of Research-ZLF, University Hospital and University Children's Hospital, University of Basel, Basel, Switz.
SOURCE: International Journal of Cancer (2002), 98(6), 930-937
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Somatostatin analogs labeled with radionuclides are of considerable interest in the diagnosis and therapy of SSTR-expressing tumors, such as gastroenteropancreatic, small cell lung, breast and frequently nervous system tumors. In view of the favorable phys. characteristics of the Ga isotopes 67Ga and 68Ga, enabling conventional tumor scintigraphy, PET and possibly internal radiotherapy, we focused on the development of a Ga-labeled somatostatin analog suitable for targeting SSTR-expressing tumors. For this purpose, 3 somatostatin analogs, OC, TOC and TATE were conjugated to the metal chelator DOTA and labeled with the radiometals 111In, 90Y and 67Ga. They were then evaluated for their performance in the AR4-2J pancreatic tumor model by testing SSTR2-binding affinity, internalization/externalization in isolated cells and biodistribution in tumor-bearing nude mice. Surprisingly, we found that, compared to 111In or 90Y, labeling with 67Ga considerably improved the biol. performance of the tested somatostatin analogs with respect to SSTR2 affinity and tissue distribution. 67Ga-labeled DOTA-somatostatin analogs were rapidly excreted from nontarget tissues, leading to excellent tumor-to-nontarget tissue uptake ratios. Of interest for radiotherapeutic application, [67Ga]DOTATOC was strongly internalized by AR4-2J cells. Furthermore, our results suggest a link between the radioligand charge and its kidney retention. The excellent tumor selectivity of Ga-DOTA somatostatin analogs together with the different applications of Ga in nuclear oncol. suggests that Ga-DOTA somatostatin analogs will become an important tool in the management of SSTR-pos. tumors.

IT **405263-92-5D**, indium-111 complex
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(67Ga- vs. 111In- and 90Y-labeled DOTA-somatostatin analogs for neuroendocrine **tumor** targeting)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:264159 HCAPLUS
DOCUMENT NUMBER: 137:33520
TITLE: Synthesis, In Vitro Receptor Binding, and In Vivo Evaluation of Fluorescein and Carbocyanine Peptide-Based Optical Contrast Agents
AUTHOR(S): Achilefu, Samuel; Jimenez, Hermo N.; Dorshow, Richard B.; Bugaj, Joseph E.; Webb, Elizabeth G.; Wilhelm, R. Randy; Rajagopalan, Raghavan; Johler, Jill; Erion, Jack L.
CORPORATE SOURCE: Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(10), 2003-2015
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Site-specific delivery of drugs and contrast agents to tumors protects normal tissues from the cytotoxic effects of drugs and enhances the contrast between normal and pathol. tissues. One approach to achieve selectivity is to target overexpressed receptors on the membranes of tumor cells and to visualize the tumors by a noninvasive optical imaging method. Accordingly, the authors conjugated fluorescein and carbocyanine dyes to somatostatin and bombesin receptor-avid peptides and examd. their receptor binding affinities. The authors also prepd. potential dual imaging probes consisting of a bioactive peptide for tumor targeting, a biocompatible dye for optical imaging, and a radioactive or paramagnetic metal chelator for scintigraphic or magnetic resonance imaging of tumors. Using these approaches, the resulting carbocyanine derivs. of somatostatin and bombesin analogs retained high binding for their resp. receptors. Further evaluation of representative mols. in rats bearing somatostatin- and bombesin-pos. tumors showed selective uptake of the agents by the tumor cells. Unlike carbocyanine derivs., the receptor binding of fluorescein-somatostatin peptide conjugates was highly sensitive to the type of linker and the site of fluorescein attachment on the nonreceptor binding region of the peptide. In general, the presence of flexible linkers disrupted binding affinity, possibly due to the interaction of the linker's thiourea group with the peptide's cyclic disulfide bond. While the receptor binding affinity of the dual probes was not dependent on the type of chelating group examd., it was affected by the relative positions of fluorescein and chelator on the lysine linker. For somatostatin compds., best results were obtained when the chelator was on the .alpha.-amino lysine linker and fluorescein was on the .epsilon.-amino group. In contrast, conjugation of the chelator to .epsilon.- and fluorescein to the .alpha.-amino lysine linker of bombesin peptides resulted in high receptor binding. These findings indicate that, despite their small size, conjugation of dyes to truncated somatostatin and bombesin peptide analogs results in promising diagnostic agents that retain high receptor binding activity in vitro. The results further show that these contrast agents can selectively and specifically localize in receptor-pos. tumors in rat models.

IT **436142-14-2P 436142-25-5P**
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn., in vitro receptor binding, and in vivo evaluation of fluorescein- and carbocyanine-**conjugates** of peptides as **tumor**-targeting optical contrast agents)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:142702 HCAPLUS
DOCUMENT NUMBER: 136:209641
TITLE: Perfluoroalkyl-containing tetraazacyclododecane metal complexes comprising sugar residues, method for their preparation and use as imaging agents
INVENTOR(S): Platzek, Johannes; Mareski, Peter; Niedballa, Ulrich; Raduechel, Bernd; Weinmann, Hanns-Joachim; Misselwitz, Bernd
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014309	A1	20020221	WO 2001-EP8499	20010723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10040381	C1	20020606	DE 2000-10040381	20000811
AU 2001089729	A5	20020225	AU 2001-89729	20010723
US 2002076379	A1	20020620	US 2001-925622	20010810

PRIORITY APPLN. INFO.: DE 2000-10040381 A 20000811
US 2000-234952P P 20000926
WO 2001-EP8499 W 20010723

OTHER SOURCE(S): MARPAT 136:209641

AB The invention relates to transition metal and rare earth complexes with tetraazacyclododecanetriactate or polyaminopolycarboxylic acids contg. perfluoroalkyl groups, sugar residues and amino acid which can be used i.v. lymphog., in tumor diagnosis and for infarct and necrosis imaging. For example, the Gd complex of 6-N-[1,4,7-tris(carboxylatomethyl)]-1,4,7,10-tetraazacyclododecane-10-N-[(pentanoyl-3-aza-4-oxo-5-methyl-5-yl)]-2-N-[1-O-.alpha.-D-carbonylmethylmannopyranose]-L-lysine-[1-(4-perfluorooctylsulfonyl)piperazine]amide was prepd. in a multistep process starting from N-benzyloxycarbonyl-L-lysine and Et trifluoroacetate, with subsequent reaction with 1-perflurooctylsulfonylpiperazine, followed by deprotection and reaction with 1-O-.alpha.-D-carboxymethyl-2,3,4,6-tetra-O-benzylmannopyranose, deprotection and reaction with gadolinium complex with 1,4,7-tris(carboxymethyl)-10-(carboxy-3-aza-4-oxo-5-methylpent-5-yl)-1,4,7,10-tetraazacyclododecane.

IT **400708-43-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reactant for prepn. of gadolinium/manganese complexes with polyaminopolycarboxylate contg. perfluoroalkyl and sugar and amino acid residues as imaging agents for use in lymphog. **tumor** diagnosis and infarct and necrosis imaging)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:125733 HCAPLUS
DOCUMENT NUMBER: 136:321356
TITLE: Chemical Synthesis of Escherichia Coli STh Analogues by Regioselective Disulfide Bond Formation: Biological Evaluation of an 111In-DOTA-Phe19-STh Analogue for Specific Targeting of Human Colon Cancers
AUTHOR(S): Gali, Hariprasad; Sieckman, Gary L.; Hoffman, Timothy J.; Owen, Nellie K.; Mazuru, Dana G.; Forte, Leonard R.; Volkert, Wynn A.
CORPORATE SOURCE: Research Service, Harry S. Truman Memorial Veterans' Administration Hospital, Columbia, MO, 65201, USA
SOURCE: Bioconjugate Chemistry (2002), 13(2), 224-231
CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB New human Escherichia coli heat-stable peptide (STh) analogs contg. a DOTA chelating group were synthesized by sequential and selective formation of disulfides bonds in the peptide. This synthetic approach utilizes three orthogonal thiol-protecting groups, Trt, Acm, and t-Bu, to form three disulfide bonds by successive reactions using 2-PDS, iodine, and silyl chloride-sulfoxide systems. The DOTA-STh conjugates exhibiting high guanylin/guanylate cyclase-C (GC-C) receptor binding affinities were obtained with >98% purity. In vitro competitive binding assays, employing T-84 human colon cancer cells, demonstrated the IC50 values of <2 nM for GC-C receptor binding suggesting that the new synthetic STh analogs are biol. active. In vitro stability studies of the 111In-DOTA-Phe19-STh conjugate incubated in human serum at 37 .degree.C under 5% CO2 atmosphere revealed that this conjugate is extremely stable with no observable decompn. at 24 h postincubation. HPLC anal. of mouse urine at 1 h pi of the 111In-DOTA-Phe19-STh conjugate showed only about 15% decompn. suggesting that the 111In-DOTA-Phe19-STh conjugate is highly stable, even under in vivo conditions. In vivo pharmacokinetic studies of the 111In-DOTA-Phe19-STh conjugate in T-84 human colon cancer derived xenografts in SCID mice conducted at 1 h pi showed an initial tumor uptake of 2.04 .+-. 0.30% ID/g at 1 h pi with efficient clearance from the blood pool (0.23 .+-. 0.14% ID/g, 1 h pi) by excretion mainly through the renal/urinary pathway (95.8 .+-. 0.2% ID, 1 h pi). High tumor/blood, tumor/muscle, and tumor/liver ratios of approx. 9:1, 68:1, and 26:1, resp., were achieved at 1 h pi The specific in vitro and in vivo uptake of the radioactivity by human colonic cancer cells highlights the potential of radiometalated-DOTA-STh conjugates as diagnostic/therapeutic radiopharmaceuticals.

IT **415697-94-8P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of 111In-DOTA-Phe19-STh analog for targeting human colon **cancer**)

IT **415697-89-1P 415697-90-4P 415697-91-5P 415697-92-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of 111In-DOTA-Phe19-STh analog for targeting human colon **cancer**)

IT **415697-93-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of 111In-DOTA-Phe19-STh analog for targeting human colon **cancer**)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:51305 HCAPLUS
DOCUMENT NUMBER: 136:123597
TITLE: Preparation of stable radiopharmaceutical compositions useful for tumor therapy
INVENTOR(S): Liu, Shuang; Barrett, John A.; Carpenter, Alan P., Jr.
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004030	A2	20020117	WO 2001-US21261	20010705

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-216396P P 20000706
OTHER SOURCE(S): MARPAT 136:123597

AB The present invention provides stable radiopharmaceutical compns. including a therapeutic radionuclide and an effective stabilizing amt. of an arom. stabilizer (e.g., a polyhydroxylated arom. compd., an arom. amine, or a hydroxylated arom. amine), alone or in combination with other antioxidants or stabilizers, to inhibit radiolytic degrdn. of radiopharmaceuticals. The present invention also provides improved radiopharmaceutical formulations by the use of an arom. stabilizing agent (e.g., a polyhydroxylated arom. compd., an arom. amines, or a hydroxylated arom. amine), and/or low temp. storage. The present invention also provides processes for making stable radiopharmaceutical compns. The present invention also provides the use of the pharmaceutical compns. in medical therapy and/or medical diagnosis.

IT **250612-82-9P 277316-41-3P 277316-45-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of chelator-optional linker-biomol. **conjugates** for use in stable radiopharmaceutical compns.)

IT **250612-07-8P 277315-68-1P 277315-72-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of chelator-optional linker-biomol. **conjugates** for use in stable radiopharmaceutical compns.)

L11 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:30997 HCAPLUS
DOCUMENT NUMBER: 136:102654
TITLE: Preparation of conjugates of peptides and lanthanide-chelates for use as fluorescence diagnostic materials in vivo or in vitro
INVENTOR(S): Bauer, Michael; Becker, Andreas; Licha, Kai; Bornhop, Darryl; Platzek, Johannes
PATENT ASSIGNEE(S): Shering Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 97 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 1170021 A2 20020109 EP 2001-250164 20010514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 2000-571407 A 20000515
OTHER SOURCE(S): MARPAT 136:102654
AB Synthesis of title compds., consisting of peptides, fragments, or analogs, composed of either D- or L-amino acids, based on vasoactive intestinal peptide, somatostatin, or neurotensin sequences, bearing chelating groups, were prepd. for use as fluorescent diagnostic materials for identification of tumors of the gastrointestinal tract, esophagus, urogenital tract, or lung. Peptide D-Phe-c[Cys-Phe-D-Trp-Lys-Thr-Cys] was conjugated to Tb complex of (S)-[(HO2CCH2)2NCH2CH2]2NCH(CH2-4-C6H4OCH2CO2H)CO2H, prepd. in three steps from (S)-[(PhCH2OC(O)CH2)2NCH2CH2]2NCH(CH2-4-C6H4OCH2CO2H)C(O)OCH2Ph, to give the title terbium complex. Similar complexes contg. europium, gadolinium, or bismuth, with cyclic or straight chain peptides, and substituted 1,4,7,10-tetraazacyclododecane chelating portions, were also prepd. Over two hundred peptide sequences were claimed as potential fragments of the title complexes.
IT **387389-45-9DP**, europium complex
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **conjugates** of peptides and lanthanide-chelates for use as fluorescence diagnostic materials in vivo or in vitro)

L11 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:935452 HCAPLUS
DOCUMENT NUMBER: 136:70083
TITLE: Pharmaceuticals for the imaging of angiogenic disorders for use in combination therapy
INVENTOR(S): Rajopadhye, Milind; Edwards, D. Scott; Barrett, John A.; Carpenter, Alan P., Jr.; Heminway, Stuart J.; Liu, Shuang; Singh, Prahlad
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 306 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001097860	A2	20011227	WO 2001-US20108	20010621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-213206P P 20000621
OTHER SOURCE(S): MARPAT 136:70083
AB Compds. (Q)d-Ln-Ch (Q is a peptide, d = 1-10, Ln is a linking group, Ch is a metal-bonding unit) were prepd. for use in the diagnosis and treatment of cancer in combination therapy in a patient. The present invention also provides novel compds. useful for the treatment of rheumatoid arthritis (no data). Thus, cyclo{Arg-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-

pyridinyl]hydrazono]methyl]benzenesulfonic acid]-3-aminopropyl)-Val} was prepd. by acylation of cyclo{Arg-Gly-Asp-D-Tyr(3-aminopropyl)-Val} with 2-[[[5-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-pyridinyl]hydrazono]methyl]benzenesulfonic acid monosodium salt and converted into radiopharmaceutical 99mTc(VnA)(tricine)(phosphine), where VnA represents the vitronectin receptor antagonist.

IT **250612-06-7P 250612-07-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of **cancer** in combination therapy)

IT **250612-82-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of **cancer** in combination therapy)

L11 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:935440 HCAPLUS
DOCUMENT NUMBER: 136:70082
TITLE: Vitronectin receptor antagonist pharmaceuticals for use in combination therapy
INVENTOR(S): Harris, Thomas D.; Barrett, John A.; Carpenter, Alan P., Jr.; Rajopadhye, Milind
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 542 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001097848	A2	20011227	WO 2001-US19793	20010621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-213210P P 20000621
OTHER SOURCE(S): MARPAT 136:70082

AB Anticancer agents of the formulas (Q)d-Ln-Ch or (Q)d-Ln-(Ch)d (I) [Q is a residue having a quinolone-type moiety; Ln is a linking group; Ch is a metal-bonding unit; d = 1-10; d' = 1-100] and kits contg. I are prepd. for the treatment of cancer in combination therapy in a patient. I are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. I may be used with radioisotopes; in addn., I may be used in conjunction with radio- and photosensitizers, ligands such as TPPTS or tricine, and reducing agents such as tin(II). The present invention provides novel compds. useful for the treatment of rheumatoid arthritis (no data).

IT **277315-66-9P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of peptide- and tetraazadodecane-contg. quinolones and their radioactive metal complexes as **anticancer** agents)

IT **277315-65-8P 277315-67-0P 277315-68-1P**
277315-69-2P 277315-70-5P 277315-72-7P
277315-76-1P 277315-77-2P 277315-79-4P
277315-80-7P 277316-60-6P 277316-61-7P
277316-62-8P 277316-63-9P 277316-64-0P
277316-65-1P 277316-66-2P 277316-67-3P
277316-68-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide- and tetraazadodecane-contg. quinolones and their radioactive metal complexes as **anticancer** agents)

IT **277316-20-8P 277316-34-4P 277316-39-9P**
277316-41-3P 277316-45-7P 277316-52-6P
277316-56-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptide- and tetraazadodecane-contg. quinolones and their radioactive metal complexes as **anticancer** agents)

L11 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:868272 HCAPLUS
DOCUMENT NUMBER: 136:11092
TITLE: Contrast agents
INVENTOR(S): Klaveness, Jo; Tolleshaug, Helge
PATENT ASSIGNEE(S): Nycomed Imaging AS, Norway
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001089584	A2	20011129	WO 2001-NO215	20010523
WO 2001089584	A3	20020502		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
NO 2000-2644	A	20000523
US 2000-210061P	P	20000607

AB This invention relates to contrast agents and the use of these contrast agents for diagnosis of diseases in humans and animals based on mapping of metabolic activity. The contrast agents can be used to identify tissue or cells with metabolic activity or enzymic activity deviating from the normal. A contrast agent substrate changes pharmacodynamic and/or

pharmacokinetic properties upon a chem. modification from a contrast agent substrate to a contrast agent product in a specific enzymic transformation, thereby detecting areas of disease upon a deviation in the enzyme activity from the normal. Examples showing prepn. of conjugates which are substrates for MMP-7, cathepsin D, esterase, transglutaminase, and caspase-3 are given, as well as methods for prepg. microbubble dispersions. The conjugates are suitable for MRI, PET and scintigraphy.

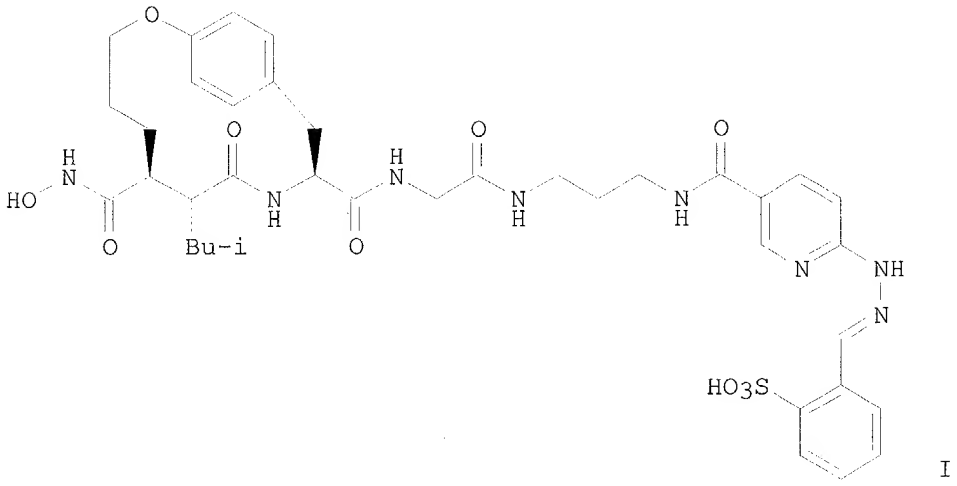
IT **374804-69-0P**
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(peptide-**conjugated** gadolinium and technetium complexes as contrast agents: prepn. and formulation as microbubbles)

L11 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:617999 HCAPLUS
DOCUMENT NUMBER: 135:180952
TITLE: Preparation of matrix metalloproteinase inhibitors
INVENTOR(S): Decicco, Carl P.; Nelson, David J.; Barrett, John A.; Carpenter, Alan P., Jr.; Duran, James J.; Rajopadhye, Milind
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 179 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060820	A2	20010823	WO 2001-US4848	20010215
WO 2001060820	A3	20020221		

W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO.: US 2000-182627P P 20000215
OTHER SOURCE(S): MARPAT 135:180952
GI



I

AB Compds. Qd-Ln-Ch (Qd is 1-10 targeting moieties; Ln is a linking group; Ch is a chelator) were prepd. The chelator is able to conjugate a cytotoxic radioisotope. The targeting moiety, e.g., R1NHCOCR2R3NR4R5 [R1 = OH or Ph, which is optionally substituted with a bond to the linking group or to the chelator, provided when R1 = Ph, R3 = 2-[(1-carboxyethyl)amino]alkanoyl; R2, R3, R4, R5 = H, C1-6, which is alkyl optionally substituted with a bond to the linking group or to the chelator; R2R3C or R4R5N may form a ring], is a matrix metalloproteinase inhibitor. Thus, peptidomimetic I was prepd. by coupling reactions of (3-aminopropyl)carbamic acid tert-Bu ester with oxaazabicyclo[10.2.2]hexadecatrienecarboxylic acid derivs. Compds. of the invention were found to be active in matrix metalloproteinase inhibitory assays.

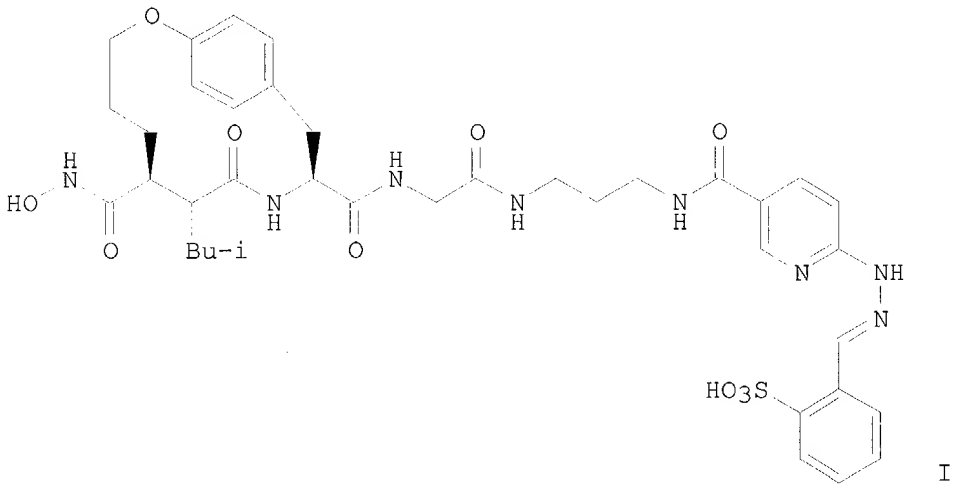
IT **355149-94-9P 355149-96-1P 355149-97-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of matrix **metalloproteinase** inhibitors)

L11 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:617870 HCAPLUS
DOCUMENT NUMBER: 135:180950
TITLE: Preparation of matrix metalloproteinase inhibitors as diagnostic agents
INVENTOR(S): Carpenter, Alan P., Jr.; Rajopadhye, Milind
PATENT ASSIGNEE(S): DuPont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 205 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060416	A2	20010823	WO 2001-US4870	20010215
WO 2001060416	A3	20020131		

W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ,

PL, RO, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR
PRIORITY APPLN. INFO.: US 2000-182712P P 20000215
OTHER SOURCE(S): MARPAT 135:180950
GI



I

AB Diagnostic agents comprising a diagnostic metal or an echogenic gas and compds. Qd-Ln-R (Qd is 1-10 targeting moieties; Ln is a linking group; R is a chelator or a surfactant) were prepd. The chelator is able to conjugate the diagnostic metal. The surfactant is capable of forming an echogenic gas filled lipid sphere or microbubble. The targeting moiety, e.g., R1NHCOCR2R3NR4R5 [R1 = OH or Ph, which is optionally substituted with a bond to the linking group or to the chelator, provided when R1 = Ph, R3 = 2-[(1-carboxyethyl)amino]alkanoyl; R2, R3, R4, R5 = H, C1-6, which is alkyl optionally substituted with a bond to the linking group or to the chelator; R2R3C or R4R5N may form a ring], is a matrix metalloproteinase inhibitor. Thus, peptidomimetic I was prepd. by coupling reactions of (3-aminopropyl)carbamic acid tert-Bu ester with oxaazabicyclo[10.2.2]hexadecatrienecarboxylic acid derivs. Compds. of the invention were found to be active in matrix metalloproteinase inhibitory assays.

IT **355149-94-9P 355149-96-1P 355149-97-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of matrix **metalloproteinase** inhibitors)

L11 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:421741 HCAPLUS
DOCUMENT NUMBER: 135:177368
TITLE: 90Y and 177Lu Labeling of a DOTA-Conjugated Vitronectin Receptor Antagonist Useful for Tumor Therapy
AUTHOR(S): Liu, Shuang; Cheung, Eric; Ziegler, Marisa C.; Rajopadhye, Milind; Edwards, D. Scott
CORPORATE SOURCE: Medical Imaging Division, DuPont Pharmaceuticals

Company, North Billerica, MA, 01862, USA
SOURCE: Bioconjugate Chemistry (2001), 12(4), 559-568
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 90Y and 177Lu complexes (RP697 and RP688, resp.) of a DOTA-conjugated vitronectin receptor antagonist (SU015: 2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-1-cyclododecyl)acetyl-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe}) were prepd. by reacting SU015 with the radiometal chloride in ammonium acetate buffer (pH > 7.2) in the presence of an antioxidant (sodium gentisate, GA). Through a series of radiolabeling expts., it was found that there are many factors influencing the rate of 90Y chelation and the radiolabeling efficiency of SU015. These include the purity of SU015, the pH, reaction temp., and heating time, as well as the presence of trace metal contaminants, such as Ca2+, Fe3+, and Zn2+. The chelation of 90Y by SU015 is slow, so that heating at elevated temps. (50-100 .degree.C) is needed to complete the 90Y-labeling. The rate of 90Y chelation is also dependent on the pH of the reaction mixt. Under optimized radiolabeling conditions (pH 7.2-7.8 and heating at 50-100 .degree.C for 5-10 min), the min. amt. of SU015 required to achieve 95% RCP for RP697 is .apprx.25 .mu.g for 20 mCi of 90YCl3 corresponding to a SU015:90Y ratio of .apprx.30:1.

IT **250612-06-7P 250612-81-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(90Y and 177Lu labeling of DOTA-**conjugated** vitronectin receptor antagonist useful for **tumor** therapy)

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:421740 HCAPLUS
DOCUMENT NUMBER: 135:185318
TITLE: Stabilization of 90Y-Labeled DOTA-Biomolecule Conjugates Using Gentisic Acid and Ascorbic Acid
AUTHOR(S): Liu, Shuang; Edwards, D. Scott
CORPORATE SOURCE: Medical Imaging Division, DuPont Pharmaceuticals Company, North Billerica, MA, 01862, USA
SOURCE: Bioconjugate Chemistry (2001), 12(4), 554-558
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Radiolytic degrdn. of radiolabeled compds. is a major challenge for the development of new therapeutic radiopharmaceuticals. The goal of this study is to explore the factors influencing the soln. stability of a 90Y-labeled DOTA-peptide conjugate (RP697), including the amt. of total activity, the activity concn., the stabilizer concn., and the storage temp. In general, the rate of radiolytic decompn. of RP697 is much slower at the lower activity concn. (<4 mCi/mL) than that at the higher concn. (>10 mCi/mL). RP697 remains relatively stable at the 20 mCi level and room temp. while it decomps. rapidly at the 100 mCi level under the same storage conditions. Radical scavengers, such as gentisic acid (GA) and ascorbic acid (AA), were used in combination with the low temp. (-78 .degree.C) to prevent the radiolytic decompn. of RP697. It was found that RP697 remains stable for at least 2 half-lives of 90Y when GA or AA (10 mg for 20 mCi of 90Y) is used as a stabilizer when the radiopharmaceutical compn. is stored at -78 .degree.C. The stabilizer (GA and AA) can be

added into the formulation either before or after radiolabeling. The post-labeling approach is particularly useful when the use of a large amt. of the stabilizer interferes with the radiolabeling. The radiopharmaceutical compn. developed in this study can also apply to other 90Y-labeled DOTA-biomol. conjugates. The amt. of the stabilizer used in the radiopharmaceutical compn. and storage temp. should be adjusted according to the sensitivity of the radiolabeled DOTA-biomol. conjugate toward radiolytic decompn.

IT **250612-06-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(stabilization of 90Y-labeled DOTA-biomol. **conjugates** using gentisic acid and ascorbic acid)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:35363 HCAPLUS
DOCUMENT NUMBER: 135:149232
TITLE: Comparative dosimetry of copper-64 and yttrium-90-labeled somatostatin analogs in a tumor-bearing rat model
AUTHOR(S): Lewis, Jason S.; Laforest, Richard; Lewis, Michael R.; Anderson, Carolyn J.
CORPORATE SOURCE: Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Cancer Biotherapy & Radiopharmaceuticals (2000), 15(6), 593-604
CODEN: CBRAFJ; ISSN: 1084-9785
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 90Y-DOTA-tyrosine3-octreotide (90Y-DOTA-Y3-OC) is currently being evaluated as a radiotherapy agent for trials in patients with somatostatin-receptor pos. cancer. In this study, the authors compared the estd. absorbed doses to human organs, as well as to a CA20948 rat tumor, of90Y- and 64Cu-labeled DOTA-Y3-OC and DOTA-Y3-octreotate (DOTA-Y3-TATE). Assuming that the radiopharmaceutical biodistributions are the same in rodents and humans, human absorbed dose ests. were obtained from rat biodistribution data. The absorbed doses of90Y-DOTA-Y3-TATE were detd. from the biodistribution of the 88Y-labeled peptide, with and without co-injection of a therapeutic amt. of the 90Y-labeled peptide. Addnl., the absorbed doses of90Y-DOTA-Y3-TATE were detd. from data using 2 different biodistribution endpoints, 48 h and 168 h. Human absorbed dose ests. were calcd. using MIRD methodol. assuming that rats and humans have the same biodistribution. The biodistribution of the radiolabeled somatostatin analogs was dependent on the peptide and the radiometal. For 90Y-DOTA-Y3-TATE, the tumor dose was dependent on both the administration of therapeutic 90Y-peptide and the biodistribution endpoint. These data suggested that, for both radionuclides, the TATE derivs. imparted a higher absorbed dose to the tumor than the OC analogs. 90Y-DOTA-Y3-OC and64Cu-DOTA-Y3-OC were comparable with respect to their tumor-to-normal tissue dose ratios, while 90Y-DOTA-Y3-TATE appeared to have distinct advantages over 64Cu-DOTA-Y3-TATE.

IT **177943-88-3D**, Cu-64 complexes **177943-88-3D**, Y-88 complexes **177943-88-3D**, Y-90 complexes **204318-14-9D**, Cu-64 complexes **204318-14-9D**, Y-88 complexes **204318-14-9D**, Y-90 complexes
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study,

unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(Cu-64 and Y-90-labeled somatostatin analogs dosimetry in a **tumor**-bearing rat model)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:661180 HCAPLUS
DOCUMENT NUMBER: 133:249059
TITLE: Radionuclide conjugates with DOTA-biotin derivatives for diagnosis and therapy
INVENTOR(S): Griffiths, Gary L.; Hansen, Hans; Govindan, Serengulam V.
PATENT ASSIGNEE(S): Immunomedics, Inc., USA
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 486,166, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6120768	A	20000919	US 1997-990843	19971215
US 5736119	A	19980407	US 1995-409960	19950323
US 5922302	A	19990713	US 1995-440652	19950515
WO 9930745	A2	19990624	WO 1998-US26579	19981215
WO 9930745	A3	20000113		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9918258	A1	19990705	AU 1999-18258		19981215
PRIORITY APPLN. INFO.:			US 1993-62662	B1	19930517
			US 1995-409960	A2	19950323
			US 1995-486166	B2	19950607
			US 1996-688781	A2	19960731
			US 1997-990843	A1	19971215
			WO 1998-US26579	W	19981215

AB A radionuclide-chelator conjugate compn. for detecting and/or treating lesions in a patient comprises pre-targeting the cell, tissue, or pathogen with a substrate, using a targeting protein that specifically binds a marker substance on the target cell, tissue, or pathogen and to which the substrate is directly or indirectly bound. Parenteral injection comprises a chelate conjugate of biotin, a chelator, and a chelatable detection or therapeutic agent, and allows the compn. to accrete at the targeted cell, tissue, or pathogen. The chelate conjugate is purified by liq. chromatog. after chelate formation, or further comprises a blood transit-modifying linker or addend that is covalently bound within the chelate conjugate, or both. The detection or therapeutic agent of the invention are used to detect or treat cancer, infectious diseases, or cardiovascular diseases. Prepn. of biotin-D-Phe-D-Lys-DOTA is presented.

IT **192221-17-3P 192221-18-4P 192221-19-5P**

245758-39-8P 294637-28-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radionuclide **conjugates** contg. DOTA-biotin derivs. for diagnosis and therapy)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:602793 HCAPLUS
DOCUMENT NUMBER: 134:127855
TITLE: OctreoTher: ongoing early clinical development of a somatostatin-receptor-targeted radionuclide antineoplastic therapy
AUTHOR(S): Smith, M. Charles; Liu, Jingou; Chen, Tianling; Schran, Horst; Yeh, Ching-Ming; Jamar, Francois; Valkema, Roelf; Bakker, Willem; Kvols, Larry; Krenning, Eric; Pauwels, Stanislas
CORPORATE SOURCE: Novartis Pharmaceuticals Corporation, East Hanover, NJ, 07936-1080, USA
SOURCE: Digestion (2000), 62(Suppl. 1), 69-72
CODEN: DIGEBW; ISSN: 0012-2823
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB OctreoTher (90Y-DOTA-D-Phe1-Tyr3-octreotide, a.k.a. 90Y-SMT 487) consists of a somatostatin peptide analog (Tyr3-octreotide), coupled with a complexing moiety (DOTA), and labeled with a tightly bound beta-emitter (yttrium-90). By targeting somatostatin receptor-pos. tumors (as imaged by OctreaScan) it may deliver a tumoricidal dose of radiation. Phase I clin. trials, conducted in patients with neuroendocrine tumors, established the safety and tolerability of the dose selected for further study and demonstrated the capacity of OctreoTher to deliver radiation doses to tumors that resulted in significant neuroendocrine tumor shrinkage. Novartis-sponsored phase II studies will soon begin to test the efficacy of OctreoTher in breast and small cell lung cancer. A fixed-dose regimen of 120 mCi/cycle .times. 3 cycles administered with concomitant amino acid infusion has been chosen for the study. Phase I data and published literature support that this fixed dose regimen will be safely tolerated.
IT **204318-14-9D**, 90Y-complexes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatostatin-receptor-targeted radionuclide **antineoplastic** therapy with OctreoTher)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:693550 HCAPLUS
DOCUMENT NUMBER: 132:9203
TITLE: DOTA-lanreotide: A novel somatostatin analog for tumor diagnosis and therapy
AUTHOR(S): Smith-Jones, Peter M.; Bischof, Claudia; Leimer, Maria; Gludovacz, Doris; Angelberger, Peter; Pangerl, Thomas; Peck-Radosavljevic, Markus; Hamilton, Gerhard; Kaserer, Klaus; Kofler, Anne; Schlagbauer-Wadl, Hermine; Traub, Tatjana; Virgolini, Irene

CORPORATE SOURCE: Departments of Nuclear Medicine, University of Vienna, Vienna, A-1090, Austria
SOURCE: Endocrinology (1999), 140(11), 5136-5148
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Long acting somatostatin-14 (SST) analogs are used clin. to inhibit tumor growth and proliferation of various tumor types via binding to specific receptors (R). We have developed a 111In-/90Y-labeled SST analog, DOTA-(D).beta.Nal1-lanreotide (DOTALAN), for tumor diagnosis and therapy. 111In-/90Y-DOTALAN bound with high affinity (dissocn. const., Kd, 1-12 nM) to a no. of primary human tumors (n = 31) such as intestinal adenocarcinoma (150-4000 fmol/mg protein) or breast cancer (250-9000 fmol/mg protein). 111In-/90Y-DOTALAN exhibited a similar high binding affinity (Kd, 1-15 nM) for the human breast cancer cell lines T47D and ZR75-1, the prostate cancer cell lines PC3 and DU145, the colonic adenocarcinoma cell line HT29, the pancreatic adenocarcinoma cell line PANC1, and the melanoma cell line 518A2. When expressed in COS7 cells, 111In-DOTALAN bound with high affinity to hsst2 (Kd, 4.3 nM), hsst3 (Kd, 5.1 nM), hsst4 (Kd, 3.8 nM), and hsst5 (Kd, 10 nM) and with lower affinity to hsst1 (Kd, .apprx.200 nM). The rank order of displacement of [125I]Tyr11-SST binding to hsst1 was: SST (IC50, 0.5 nM) .mchgt. DOTALAN (IC50, 154 nM) > lanreotide (LAN) .apprx. Tyr3-octreotide (TOCT) .apprx. DOTA-Tyr3-octreotide (DOTATOCT) .apprx. DOTA-vapreotide (DOTAVAP; IC50, >1000 nM); that to hsst2 was: DOTATOCT .apprx. TOCT .apprx. DOTALAN .apprx. SST .apprx. LAN .apprx. DOTAVAP (IC50, 1.4 nM); that to hsst3 was: SST (IC50, 1.2 nM) > DOTALAN = LAN (IC50, 15 nM) .apprx. TOCT (IC50, 20 nM) .apprx. DOTAVAP (IC50, 28 nM) > DOTATOCT (IC50, 73 nM); that to hsst4 was: SST (IC50, 1.8 nM) .apprx. DOTALAN (IC50, 2.5 nM) > LAN (IC50, 22 nM) .mchgt. DOTATOCT .apprx. DOTAVAP .apprx. TOCT (IC50, >500 nM); and that to hsst5 was: DOTALAN (IC50, 0.45 nM) > SST (IC50, 0.9 nM) > TOCT (IC50, 1.5 nM) > DOTAVAP (IC50, 5.4 nM) .mchgt. LAN (IC50, 21 nM) > DOTATOCT (IC50, 260 nM). In Sprague Dawley rats, 90Y-DOTALAN was rapidly cleared from the circulation and concd. in hsst-pos. tissues such as pancreas or pituitary. Taken together, our results indicate that 111In-/90Y-DOTALAN binds to a broad range of primary human tumors and tumor cell lines, probably via binding to hsst2.5. We conclude that this radiolabeled peptide can be used for hsst-mediated diagnosis (111In-DOTALAN) as well as systemic radiotherapy (90Y-DOTALAN) of human tumors.

IT **204318-14-9 251553-64-7**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(DOTA-lanreotide in **tumor** diagnosis and therapy and receptor specificity therein)

IT **213187-44-1**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(DOTA-lanreotide in **tumor** diagnosis and therapy and receptor specificity therein)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:442438 HCAPLUS
DOCUMENT NUMBER: 131:239827
TITLE: Radiometal-labelled macrocyclic chelator-derivatized somatostatin analogue with superb tumour-targeting properties and potential for receptor-mediated

internal radiotherapy
AUTHOR(S): Heppeler, A.; Froidevaux, S.; Macke, H. R.; Jermann, E.; Behe, M.; Powell, P.; Hennig, M.
CORPORATE SOURCE: Institute of Nuclear Medicine, Div. of Radiological Chemistry, University Hospital Basel, Basel, CH-4031, Switz.
SOURCE: Chemistry--A European Journal (1999), 5(7), 1974-1981
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A monoreactive DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid) prochelator (4,7,10-tricarboxymethyl-tert-Bu ester 1,4,7,10-tetraazacyclododecane-1-acetate) was synthesized which is useful in solid-phase and soln.-phase peptide synthesis; it was coupled to the somatostatin analog Tyr3-Lys5(BOC)-octreotide. Deprotection in one step afforded DOTA0-D-Phe1-Tyr3-octreotide (DOTATOC) in .apprxeq.65% yield. This peptide, modified with a chelator, was complexed with the radiometals 67Ga3+, 111In3+ and 90Y3+ in high yields and with high specific activities. The three radiopeptides show high stability in human serum and high affinity to the somatostatin receptor: it is four to five times higher for 67Ga-DOTATOC compared to 90Y-DOTATOC and 111In-DOTATOC. The 67Ga-labeled compd. also shows significantly higher tumor and lower kidney uptake than the two congeners. 67Ga-DOTATOC was compared in patients with the com. available gold std. 111In-DTPA0-D-Phe1-octreotide. The new compd. delineates SRIF-receptor pos. tumors very favorably and shows distinctly lower uptake by the kidneys. Evidently, the differences in the coordination chem. of the metals causes the differences in the biol. behavior. Indeed, a crystallog. study of the Ga3+ and Y3+ complexes of the model peptide DOTA-D-PheNH2 showed differences in the geometry of the complexes. The gallium complex is hexacoordinated with pseudooctahedral cis geometry and a folded macrocyclic unit. The equatorial plane is formed by two transannular nitrogens of the cyclen ring and two oxygens of the corresponding carboxylate groups. The two axial positions are formed by the two remaining ring nitrogen atoms. The amide carboxy oxygen is not bound to the metal and one carboxylate group is free and most likely contributes to the favorable handling of the radiopeptide by the kidneys. In contrast, the structure of Y-DOTA-D-PheNH2 has eight-fold coordination, and includes the amide carboxy oxygen. The geometry is a compact and somewhat distorted square-antiprism with two almost perfect planes (N4 and O4) with a max. deviation of 0.025 A. The dihedral angle between the two planes is only 0.36.degree..
IT **204318-14-9P 244219-77-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radiometal-labeled macrocyclic chelator-derivatized somatostatin analog with **tumor**-targeting properties)
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:313313 HCAPLUS
DOCUMENT NUMBER: 131:127216
TITLE: Enzymatic Cleavage of Peptide-Linked Radiolabels from Immunoconjugates
AUTHOR(S): Peterson, James J.; Meares, Claude F.
CORPORATE SOURCE: Department of Chemistry, University of California, Davis, CA, 95616-5295, USA
SOURCE: Bioconjugate Chemistry (1999), 10(4), 553-557

CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have incorporated peptides selected by combinatorial library [Peterson, J. J., and Meares, C. F. (1998) Bioconjugate Chem. 9, 618-626] into peptide-linked radiolabeled immunoconjugates of the form DOTA-peptide-antibody. Decapeptide linkers -GFQGVQFAGF- and -GFGSVQFAGF-, selected for cleavage by human liver cathepsin B, were rapidly digested in vitro when compared to the simple model tetrapeptide motif of the prototype -GGGF- [Li, M., and Meares, C. F. (1993) Bioconjugate Chem. 4, 275-283]. Cleavage properties of these library-selected substrates for cathepsin B compared favorably with decapeptide linkers -GLVGGAGAGF- and -GGFLGLGAGF-, which incorporate two of the most labile extended cathepsin B substrates from the literature. The decapeptide linker -GFGSTFFAGF-, selected from the library for cleavage by human liver cathepsin D, was rapidly digested by cathepsin D while the others were not.
IT **149206-88-2DP**, 90Y-labeled **immunoconjugates**
234442-93-4DP, 90Y-labeled **immunoconjugates**
234442-94-5DP, 90Y-labeled **immunoconjugates**
234442-95-6DP, 90Y-labeled **immunoconjugates**
234442-96-7DP, 90Y-labeled **immunoconjugates**
234442-97-8DP, 90Y-labeled **immunoconjugates**
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(prepn. of 90Y-labeled DOTA-peptide-antibody **conjugates** and cleavage by cathepsin)
IT **221328-05-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of 90Y-labeled DOTA-peptide-antibody **conjugates** and cleavage by cathepsin)
IT **234442-92-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 90Y-labeled DOTA-peptide-antibody **conjugates** and cleavage by cathepsin)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:20744 HCAPLUS
DOCUMENT NUMBER: 130:248789
TITLE: Optimized conditions for chelation of yttrium-90-DOTA immunoconjugates
AUTHOR(S): Kukis, David L.; DeNardo, Sally J.; DeNardo, Gerald L.; O'Donnell, Robert T.; Meares, Claude F.
CORPORATE SOURCE: Section of Radiodiagnosis and Therapy, Department of Internal Medicine, University of California Davis Medical Center, Sacramento, CA, USA
SOURCE: Journal of Nuclear Medicine (1998), 39(12), 2105-2110
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Radioimmunotherapy (RIT) with 90Y-labeled immunoconjugates has shown promise in clin. trials. The macrocyclic chelating agent 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA) binds 90Y with extraordinary stability, minimizing the toxicity of 90Y-DOTA

immunoconjugates arising from loss of 90Y to bone. However, reported 90Y-DOTA immunoconjugate product yields have been typically only .ltoreq.50%. Improved yields are needed for RIT with 90Y-DOTA immunoconjugates to be practical. (S) 2-[p-(bromoacetamido)benzyl]-DOTA (BAD) was conjugated to the monoclonal antibody Lym-1 via 2-iminothiolane (2IT). The immunoconjugate product, 2IT-BAD-Lym-1, was labeled in excess yttrium in various buffers over a range of concns. and pH. Kinetic studies were performed in selected buffers to est. radiolabeling reaction times under prospective radiopharmacy labeling conditions. The effect of temp. on reaction kinetics was examd. Optimal radiolabeling conditions were identified and used in eight radiolabeling expts. with 2IT-BAD-Lym-1 and a second immunoconjugate, DOTA-peptide-chimeric L6, with 248-492 MBq (6.7-13.3 mCi) of 90Y. Ammonium acetate buffer (0.5 M) was assocd. with the highest uptake of yttrium. On the basis of kinetic data, the time required to chelate 94% of 90Y (four half-times) under prospective radiopharmacy labeling conditions in 0.5 M ammonium acetate was 17-148 min at pH 6.5, but it was only 1-10 min at pH 7.5. Raising the reaction temp. from 25.degree.C to 37.degree.C markedly increased the chelation rate. Optimal radiolabeling conditions were identified as: 30-min reaction time, 0.5 M ammonium acetate buffer, pH 7-7.5 and 37.degree.C. In eight labeling expts. under optimal conditions, a mean product yield (.+-. s.d.) of 91% .+-. 8% was achieved, comparable to iodination yields. The specific activity of final products was 74-130 MBq (2.0-3.5 mCi) of 90Y per mg of monoclonal antibody. The immunoreactivity of 90Y-labeled immunoconjugates was 100% .+-. 11%. The optimization of 90Y-DOTA chelation conditions represents an important advance in 90Y RIT because it facilitates the dependable and cost-effective prepn. of 90Y-DOTA pharmaceuticals.

IT **149206-88-2DP, conjugate** with monoclonal antibody
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(optimized conditions for chelation of yttrium-90-DOTA **immunoconjugates**)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:438091 HCAPLUS
DOCUMENT NUMBER: 129:257023
TITLE: The somatostatin receptor-targeted radiotherapeutic [90Y-DOTA-dPhe1,Tyr3]octreotide (90Y-SMT 487) eradicates experimental rat pancreatic CA 20948 tumors
AUTHOR(S): Stolz, Barbara; Weckbecker, Gisbert; Smith-Jones, Peter M.; Albert, Rainer; Raulf, Friedrich; Bruns, Christian
CORPORATE SOURCE: Novartis Pharma AG, Basel, Switz.
SOURCE: European Journal of Nuclear Medicine (1998), 25(7), 668-674
CODEN: EJNMD9; ISSN: 0340-6997
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Somatostatin receptor-expressing tumors are potential targets for therapy with radiolabeled somatostatin analogs. We have synthesized a no. of such analogs in the past and identified [DOTA-dPhe1, Tyr3]octreotide (SMT 487) as the most promising candidate mol. because of its advantageous properties in cellular and in vivo tumor models. In the current paper we describe the radiotherapeutic effect of yttrium-90 labeled SMT 487 in Lewis rats bearing the somatostatin receptor-pos. rat pancreatic tumor CA

20948. SMT 487 binds with nanomolar affinity to both the human and the rat somatostatin receptor subtype 2 (sst2) (human sst2 IC50=0.9 nM, rat sst2 IC50=0.5 nM). In vivo, 90Y-SMT 487 distributed rapidly to the sst2 expressing CA 20948 rat pancreatic tumor, with a tumor-to-blood ratio of 49.15 at 24 h post injection. A single i.v. administration of 10 mCi/kg 90Y-SMT 487 resulted in a complete remission of the tumors in five out of seven CA 20948 tumor-bearing Lewis rats. No regrowth of the tumors occurred 8 mo post injection. Control animals that were treated with 30 .mu.g/kg of unlabeled SMT 487 had to be sacrificed 10 days post injection due to excessive growth or necrotic areas on the tumor surface. Upon re-inoculation of tumor cells into those rats that had shown complete remission, the tumors disappeared after 3-4 wk of moderate growth without any further treatment. The present study shows for the first time the curative potential of 90Y-SMT 487-based radiotherapy for somatostatin receptor-expressing tumors. Clin. phase I studies with yttrium-labeled SMT 487 have started in Sept. 1997.

IT **209277-09-8D**, Y-90 complexes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatostatin receptor-targeted radiotherapeutic 90Y-SMT 487 eradicates pancreatic **tumors**)

L11 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:348152 HCAPLUS
DOCUMENT NUMBER: 129:81945
TITLE: Direct synthesis of [DOTA-DPhe1]-octreotide and [DOTA-DPhe1,Tyr3]-octreotide (SMT487): two conjugates for systemic delivery of radiotherapeutical nuclides to somatostatin receptor positive tumors in man
AUTHOR(S): Albert, Rainer; Smith-Jones, Peter; Stolz, Barbara; Simeon, Corinne; Knecht, Hellmut; Bruns, Christian; Pless, Janos
CORPORATE SOURCE: Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(10), 1207-1210
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Direct attachment of unprotected DOTA (1,4,7,10-tetraazacyclododecane-N',N'',N''',N''''-tetraacetic acid) to partially suitably protected octreotide or [Tyr3]-octreotide leads after deprotection to [DOTA-DPhe1]-octreotide and [DOTA-DPhe1,Tyr3]-octreotide. These DOTA-contg. somatostatin analogs, when labeled with a radiotherapeutic nuclide, are useful as antitumor agents. The partially protected peptides are accessible via solid phase peptide synthesis (SPPS) followed by selective cleavage under mild acidic conditions from the resin.

IT **204318-14-9P 209277-09-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of DOTA-octreotide **conjugates** for systemic delivery of radiotherapeutical nuclides to somatostatin receptor pos. **tumors**)

L11 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:98351 HCAPLUS
DOCUMENT NUMBER: 128:172129

TITLE: Improved detection and therapy of lesions with biotin-chelate conjugates
INVENTOR(S): Griffiths, Gary L.; Hansen, Hans J.; Karacay, Habibe
PATENT ASSIGNEE(S): Immunomedics, Inc., USA; Griffiths, Gary L.; Hansen, Hans J.; Karacay, Habibe
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804293	A1	19980205	WO 1997-US13285	19970731
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9740474	A1	19980220	AU 1997-40474	19970731
PRIORITY APPLN. INFO.:			US 1996-688781 A2	19960731
			WO 1997-US13285 W	19970731

AB An improved method of detecting and/or treating lesions in a patient in which a pre-targeting approach is used wherein the total amt. of radionuclide delivered to a target cell, tissue, or pathogen is dramatically increased. In this method, the chelate conjugate may be purified by chromatog. after chelate formation, may contain multiple chelates or a blood transit-modifying linker or added within the chelate conjugate, or both; or a combination of these. The improved chelate conjugates can be used as detection of therapeutic agents to detect or treat the targeted cell, tissue, or pathogen. Biotin-D-Phe-D-Lys-DOTA was prepd. and complexed with gadolinium for MRI.

IT **202932-51-2DP**, complexes with radionuclides
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(detection and therapy of lesions with biotin-chelate **conjugates**)

L11 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:579696 HCAPLUS
DOCUMENT NUMBER: 127:228839
TITLE: Pharmaceutical agents containing perfluoroalkyl-containing metal complexes and the use thereof in tumor therapy and intervention al radiology
INVENTOR(S): Platzek, Johannes; Niedballa, Ulrich; Raduchel, Bernd; Schlecker, Wolfgang; Weinmann, Hanns-Joachim; Frenzel, Thomas
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9730969	A1	19970828	WO 1997-EP684	19970214
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19608278	A1	19970828	DE 1996-19608278	19960223
CA 2247253	AA	19970828	CA 1997-2247253	19970214
AU 9717692	A1	19970910	AU 1997-17692	19970214
EP 882010	A1	19981209	EP 1997-903278	19970214
EP 882010	B1	20010502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000504736	T2	20000418	JP 1997-529766	19970214
AT 200894	E	20010515	AT 1997-903278	19970214
ES 2158493	T3	20010901	ES 1997-903278	19970214
US 6180113	B1	20010130	US 1997-801983	19970219
ZA 9701537	A	19971030	ZA 1997-1537	19970221
NO 9803875	A	19981022	NO 1998-3875	19980821

PRIORITY APPLN. INFO.: DE 1996-19608278 A 19960223
US 1996-12506P P 19960229
WO 1997-EP684 W 19970214

OTHER SOURCE(S): MARPAT 127:228839

AB The invention relates to pharmaceutical agents contg. perfluoro alkylated metal complexes RF-L-A and the use thereof in tumor therapy and interventional radiol., in which formula RF is a perfluorinated, straight-chain or branched C chain with the formula -CnF2nX (X = terminal F, Cl, Br, I or H atom and n = 4-30), L is a binding group, and A is a metal complex or the salts thereof of org. and/or inorg. bases or amino acids or amino acid amides. Thus Gd/Dy/Y/Mn complexes of tetraazacyclododecane having amide pendants with perfluoroalkyl groups or polyaminopolycarboxylic acids with pendants contg. perfluoroalkyl groups were prepd.

IT **193528-92-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(for prepn. of rare earth/manganese fluoroalkyl-contg. polyaminopolycarboxylate/tetraazacyclododecane complexes for use as pharmaceutical agents in **tumor** therapy and interventional radiol.)

L11 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:433657 HCAPLUS
DOCUMENT NUMBER: 127:92211
TITLE: Development of a Streptavidin-Anti-Carcinoembryonic Antigen Antibody, Radiolabeled Biotin Pretargeting Method for Radioimmunotherapy of Colorectal Cancer. Reagent Development
AUTHOR(S): Karacay, Habibe; Sharkey, Robert M.; Govindan, Serengulam V.; McBride, William J.; Goldenberg, David M.; Hansen, Hans J.; Griffiths, Gary L.
CORPORATE SOURCE: Immunomedics Inc., Morris Plains, NJ, 07950, USA
SOURCE: Bioconjugate Chemistry (1997), 8(4), 585-594
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB With "pretargeting", radioisotope delivery to tumor is decoupled from the long antibody localization process, and this can increase tumor:blood ratios dramatically. Several reagents were prepd. for each step of a "two-step" pretargeting method, and their properties were investigated. For pretargeting tumor, streptavidin-monoclonal antibody (StAv-mab) conjugates were prepd. by crosslinking sulfo-SMCC-derivatized streptavidin to a free thiol (SH) group on MN-14 [a high-affinity anti-carcinoembryonic antigen (CEA) mab]. Thiolated mabs were generated either by reaction of 2-iminothiolane (2-IT) with mab lysine residues or by redn. of mab disulfide bonds with (2-mercaptoethyl)amine (MEA). Both procedures gave protein-protein conjugates isolated in relatively low yields (20-25%) after preparative size-exclusion (SE) chromatog. purifn. with conservative peak collection. Both StAv-MN-14 conjugates retained their ability to bind to CEA, to an anti-idiotypic antibody to MN-14 (WI2), and to biotin, as demonstrated by SE-HPLC. Two clearing agents, WI2 mab and a biotin-human serum albumin (biotin-HSA) conjugate, were developed to remove excess circulating StAv-MN-14 conjugates in animals. Both clearing proteins were also modified with galactose residues, introduced using an activated thioimidate deriv., to produce clearing agents which would clear rapidly and clear primary mab rapidly. At least 14 galactose residues on WI2 were required to reduce blood levels to 5.9 .+-. 0.7% ID/g in 1 h. Faster blood clearance (0.7 .+-. 0.2% ID/g) was obsd. in 1 h using 44 galactose units per WI2. For the delivery of radioisotope to tumor, several biotinylated conjugates consisting of biotin, a linker, and a chelate were prepd. Conjugates showed good in vitro and in vivo stability when D-amino acid peptides were used as linkers. Biotin-peptide-DOTA-indium-111 had a slightly longer blood circulation time (0.09 .+-. 0.02% ID/g in 1 h) than biotin-peptide-DTPA-indium-111 (0.05 .+-. 0.03% ID/g in 1 h) in nude mice. A longer circulation time with the neutral DOTA complex might allow higher tumor uptake.

IT **192221-17-3P 192221-18-4P 192221-19-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; streptavidin-anticarcinoembryonic antigen antibody, radiolabeled biotin pretargeting for radioimmunotherapy of colorectal **cancer**)

IT **192221-17-3DP**, In-111 complexes **192221-18-4DP**, In-111 complexes **192221-19-5DP**, In-111 complexes
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(streptavidin-anticarcinoembryonic antigen antibody, radiolabeled biotin pretargeting for radioimmunotherapy of colorectal **cancer**)

L11 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:325414 HCAPLUS
DOCUMENT NUMBER: 126:340528
TITLE: A study on pre-labeling method of monoclonal antibody Lym-1 with yttrium-90
AUTHOR(S): Zhong, Gaoren; Zhu, Jianhua; Zhu, Tong
CORPORATE SOURCE: Shanghai Medical University, Shanghai, 200032, Peop. Rep. China
SOURCE: Hejishu (1996), 19(7), 440-444
CODEN: NUTEDL; ISSN: 0253-3219
PUBLISHER: Kexue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A pre-labeling method of monoclonal antibody Lym-1 with 90Y using a new

bifunctional chelating agent (DOTA-peptide) was studied. 90Y was first labeled to the bifunctional chelating agent and then conjugated to the monoclonal antibody. The radioactivity yield was 30%. The radiochem. purity of 90Y-labeled Lym-1 was detd. to be over 95% by gel filtration HPLC and silica gel TLC. The immunoreactivity of the final product was found to be greater than 100% relative to 125I-Lym-1 (as a std.) by in vitro cell binding assay.

IT **149206-88-2DP, conjugates** with monoclonal antibodies and yttrium-90
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(prelabeling method of monoclonal antibody Lym-1 with yttrium-90 using DOTA-peptide as bifunctional chelating agent)

L11 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:377062 HCAPLUS
DOCUMENT NUMBER: 125:59133
TITLE: Preparation of DOTA-containing peptides and radionucleotide complexes as antitumor agents
PATENT ASSIGNEE(S): Sandoz A.-G., Switz.
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08081498	A2	19960326	JP 1995-227906	19950905
JP 3054346	B2	20000619		
FI 9504147	A	19960307	FI 1995-4147	19950904
NO 9503457	A	19960307	NO 1995-3457	19950904
AU 9530414	A1	19960321	AU 1995-30414	19950904
AU 703057	B2	19990311		
EP 714911	A2	19960605	EP 1995-810545	19950904
EP 714911	A3	19960821		
EP 714911	B1	20010307		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 72895	A2	19960628	HU 1995-2577	19950904
HU 218284	B	20000728		
IL 115154	A1	20000813	IL 1995-115154	19950904
CZ 287012	B6	20000816	CZ 1995-2263	19950904
RU 2156774	C2	20000927	RU 1995-114740	19950904
AT 199561	E	20010315	AT 1995-810545	19950904
ES 2157309	T3	20010816	ES 1995-810545	19950904
PL 182434	B1	20020131	PL 1995-310274	19950904
CA 2157530	AA	19960307	CA 1995-2157530	19950905
CN 1127259	A	19960724	CN 1995-115610	19950905
BR 9503936	A	19960924	BR 1995-3936	19950905
ZA 9507475	A	19970306	ZA 1995-7475	19950906

PRIORITY APPLN. INFO.: GB 1994-17873 A 19940906
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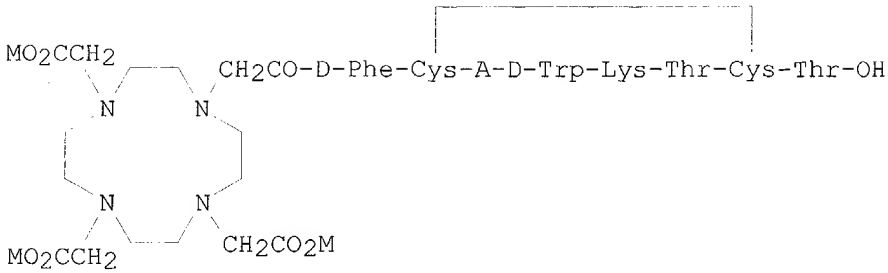


I

AB The title N-[4,7,8-tris(carboxymethyl)-4,7,10-tetraazacyclododecan-1-methylcarbonyl]somatostatin peptides (I; M = cation; A = Phe, Tyr) or their complexes with 90Y or 161Tb are prepd. A pharmaceutical compn. for treating somatostatin pos. tumors or metastasized cancers comprises .gtoreq.1 of said radionucleotide complexes or pharmaceutically acceptable salts thereof and optionally a stabilizer selected from serum albumin, ascorbic acid, retinol, gentisic acid or its deriv., and an amino acid soln. Thus, 6 g DOTA.2H2O was dissolved in 50 mL H2O, dild. with 60 mL DMF, treated with 1 g N-hydroxysuccinimide, 2.7 g DCC, and [Tyr3,Lys5(Boc)]octreotide, and stirred at room temp. for 72 h to give, after deprotection with CF3CO2H, the title peptide I acetic acid salt (M = H, A = Phe). To a soln. of the latter compd. (50 .mu.M, 20 .mu.L, 0.15 M NH4OAc, 0.3 BSA, pH 4.5) was added a soln. of 90Y (1.2 mCi, 0.04 M HCl, 20 .mu.L) and the soln. was incubated at 100.degree. for 15 h and dild. with a 4 mM soln. of I (M = H, A = Phe) (pH 4.5) to give a soln. of I (M = H, A = Phe)-90Y chelate of >99.5% radiochem. purity., which was stable for 7 days.

IT **177943-88-3P 177943-89-4P 177943-91-8P**
177943-92-9P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of DOTA-contg. peptides and radionucleotide complexes as **antitumor** agents for treating somatostatin pos. **tumor** and metastasized **tumors**)

L11 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:367647 HCAPLUS
DOCUMENT NUMBER: 125:29269
TITLE: Chitosan oligomer derivatives labeled with Gd-DTPA for use as magnetic resonance contrast agents
INVENTOR(S): Hashiguchi, Yuji; Sugino, Hideki; Kamimura, Kenji; Seri, Shigemi
PATENT ASSIGNEE(S): Nihon Medi-Physics Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 707857	A1	19960424	EP 1995-116485	19951019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				

JP 08208525	A2	19960813	JP 1995-293463	19951017
JP 3170192	B2	20010528		
CA 2160819	AA	19960422	CA 1995-2160819	19951018
FI 9504967	A	19960422	FI 1995-4967	19951018
ZA 9508789	A	19960529	ZA 1995-8789	19951018
US 5863518	A	19990126	US 1995-544548	19951018
IL 115670	A1	19991130	IL 1995-115670	19951018
NO 9504183	A	19960422	NO 1995-4183	19951019
AU 9534362	A1	19960502	AU 1995-34362	19951019
AU 688119	B2	19980305		
NO 9802233	A	19960422	NO 1998-2233	19980515

PRIORITY APPLN. INFO.: JP 1994-282800 A 19941021

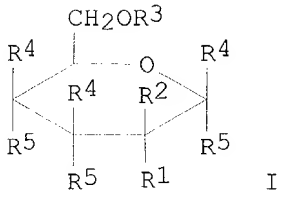
AB A diagnostic imaging agent is disclosed which comprises a compd. in which .gtoreq.1 bifunctional ligand is chem. bonded to an amino group of amino oligosaccharide having mol. wt. 500-2000 and having a redn.-treated reducing end of a sugar chain, or to an aldehyde group of a dialdehyde-oligosaccharide, .gtoreq.1 constituent monosaccharide of which is oxidn.-cleaved, having mol. wt. 500-2000 and having a redn.-treated reducing end of a sugar chain, and the ligand being coordinated with .gtoreq.1 metal ion selected from the group consisting of metal ions having the at. no. of 21-29, 31, 32, 37-39, 42-44, 49 and 56-83. Prepn. of e.g. a reduced chitosan pentamer conjugate with a gadolinium-DTPA complex is described.; the compd. was used in imaging with a rat having hepatocyte cancer.

IT **149979-17-9DP**, 1,4,7,10-Tetraazacyclododecane-1-aminoethylcarbamoylmethyl-4,7,10-tris[(R,S)-methylacetic acid], **conjugates** with maltotetraitol, bismuth complexes
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oligosaccharide **conjugate** with ligand-metal complex for MRI contrast agent)

L11 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:254285 HCAPLUS
DOCUMENT NUMBER: 124:311363
TITLE: Hydrophilic polymer and radioactive metal complexes as locally administered radio-therapeutic agents for treatment of cancer and inflammatory diseases
INVENTOR(S): Seki, Ikuya; Sato, Toku; Seri, Shigemi; Washino, Hiroaki
PATENT ASSIGNEE(S): Nihon Mediphysics Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08012597	A2	19960116	JP 1993-290080	19931026

GI



I

AB Biodegradable hydrophilic polymers (polysaccharides and their derivs. contg. 1-4 hydrophilic monomer I, with av. mol. wt. 1 x 103-1 x 106; R1, R2 = H, amino, or hydroxy group; R3 = H, glycol, or carboxymethyl group; R4, R5 = H or hydroxy group) and complex with 1 or >1 radioactive metals are claimed as locally administered radio-therapeutic agents for treatment of cancer and inflammatory diseases. Thus, I were prepd. and their pharmacokinetics and antitumor and antiinflammatory effects were studied in mice and rats and discussed with their clin. effectiveness.

IT **175892-38-3DP**, complex with indium-111
RL: BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(hydrophilic polymer and radioactive metal complexes as locally administered radio-therapeutic agents for treatment of **cancer** and inflammatory diseases)

IT **149979-17-9**, DO 3MA
RL: RCT (Reactant)
(hydrophilic polymer and radioactive metal complexes as locally administered radio-therapeutic agents for treatment of **cancer** and inflammatory diseases)

IT **175892-38-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(hydrophilic polymer and radioactive metal complexes as locally administered radio-therapeutic agents for treatment of **cancer** and inflammatory diseases)

L11 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:616058 HCAPLUS
DOCUMENT NUMBER: 123:137600
TITLE: Pharmacokinetics of chimeric L6 conjugated to indium-111- and yttrium-90-DOTA-peptide in tumor-bearing mice
AUTHOR(S): DeNardo, Sally J.; Zhong, Gao-Ren; Salako, Qansy; Li, Min; DeNardo, Gerald L.; Meares, Claude F.
CORPORATE SOURCE: Department Internal Medicine, University of California, Davis, CA, USA
SOURCE: J. Nucl. Med. (1995), 36(5), 829-36
CODEN: JNMEAQ; ISSN: 0161-5505
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A bifunctional chelating agent, DOTA-Gly3-L-(p-isothiocyanato)-phenylalanine amide (DOTA-peptide-NCS), was studied in nude mice bearing human breast cancer xenographs (HBT 3477) to det. its potential for radioimmunoconjugate therapy. Indium-111 and yttrium-90 were attached to an anti-adenocarcinoma chimeric L6 (ChL6) monoclonal antibody (MAb) after pre-chelation to the DOTA-peptide-NCS and the desired neutral radiochelates were obtained by purifn. The unique characteristic of the DOTA-peptide-NCS to form neutral complexes with trivalent metals was

utilized to sep. the resulting 111In and 90Y radiochelates from excess chelating agent and other anionic byproducts resulting from metal impurities. The purified radiochelates were then conjugated to ChL6. The pharmacokinetics of 111In- and 90Y-DOTA-peptide-ChL6 were obtained for 5 days after injection in nude mice bearing HBT 3477 xenographs. The results were compared with the pharmacokinetics of 125I-ChL6 obtained in the same mouse model. The whole-body clearance of 125I-ChL6, 90Y- and 111In-DOTA-peptide-ChL6 was monoexponential with biol. half-times of 92, 104 and 160 h, resp. Blood clearances of the three radiopharmaceuticals were biphasic. The radiometal immunoconjugates had greater tumor uptake and slower clearances. Indium-111- and 90Y-DOTA-peptide-ChL6 can be produced at high specific activity with fewer than one chelate per MAb by using a pre-labeling method that permits radiochelate purifn. by charge selection. Studies in mouse xenografts indicate that tumor uptake is enhanced and a favorable therapeutic index is achieved using these agents.

IT **149206-88-2D**, complexes with radionuclides and chimeric L6 monoclonal antibody
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmacokinetics of chimeric L6 **conjugated** to indium-111- and yttrium-90-DOTA-peptide in **tumor**-bearing mice)

L11 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:200413 HCAPLUS
DOCUMENT NUMBER: 120:200413
TITLE: Labeling Monoclonal Antibodies with 90Yttrium- and 111Indium-DOTA Chelates: A Simple and Efficient Method
AUTHOR(S): Li, Min; Meares, Claude F.; Zhong, Gao-Ren; Miers, Laird; Xiong, Cheng-Yi; DeNardo, Sally J.
CORPORATE SOURCE: Department of Chemistry, University of California, Davis, CA, 95616, USA
SOURCE: Bioconjugate Chem. (1994), 5(2), 101-4
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Yttrium-90 and indium-111 have been attached to a monoclonal antibody with a bifunctional chelating agent (DOTA-peptide). Using the unique features of this DOTA-peptide and its complexes with trivalent yttrium and indium, the bifunctional chelating agent was prelabeled with either radiometal and then conjugated to chimeric monoclonal antibody L6. Both radiolabeling procedures and yield are suitable for the practical prepn. of radiopharmaceuticals. Biodistribution studies in tumor-bearing mice showed that, e.g., on day 3 after i.v. injection of a 90Y immunoconjugate, liver uptake was 5.4 .+-. 1.5% ID/g, bone uptake 2.0 .+-. 0.5% ID/g, and tumor uptake 18.0 .+-. 8.0% ID/g.

IT **149206-88-2DP**, complexes with indium-111 and yttrium-90, **conjugates** with monoclonal antibodies
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and biodistribution of, as radiopharmaceuticals)

L11 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:620702 HCAPLUS
DOCUMENT NUMBER: 119:220702
TITLE: Dendrimeric polychelants as imaging agents
INVENTOR(S): Watson, Alan D.
PATENT ASSIGNEE(S): Cockbain, Jilian Roderick Michaelson, UK; Nycomed Salutar, Inc.
SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9306868	A1	19930415	WO 1992-EP2308	19921006
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9226757	A1	19930503	AU 1992-26757	19921006
AU 671601	B2	19960905		
EP 607222	A1	19940727	EP 1992-920822	19921006
EP 607222	B1	19981223		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
JP 07503031	T2	19950330	JP 1992-506624	19921006
AT 174800	E	19990115	AT 1992-920822	19921006

PRIORITY APPLN. INFO.: US 1991-772349 19911007
WO 1992-EP2308 19921006

AB Polyvalent chelating agents, comprising multiple macrocyclic chelating moieties conjugated to a .ltoreq.5th-generation dendrimer backbone, and their metal chelates are useful in diagnostic imaging and radiotherapy. To produce a site-specific agent, .gtoreq.1 of the chelating agent-carrying backbone mols. may be conjugated to a site-directed mol., e.g. a protein. Thus, Me acrylate reacted with NH3-MeOH to form N(CH2CH2CO2Me)3, which combined with H2NCH2CH2NH2 to form a 1st-generation polyaminoamido starburst dendrimer; further generations were produced by alternate reaction of the product with Me acrylate and H2NCH2CH2NH2. A 2nd-generation dendrimer was coupled to 12 equiv. of DOTA carboxycarbonic anhydride, complexed with Gd, and conjugated via succinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate to 2-iminothiolane-activated antibody L6.

IT **150467-20-2D, conjugates** with starburst dendritic polymers, metal complexes
RL: BIOL (Biological study)
(for diagnostic imaging and radiotherapy)

L11 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:490207 HCAPLUS
DOCUMENT NUMBER: 119:90207
TITLE: Synthesis, metal chelate stability studies, and enzyme digestion of a peptide-linked DOTA derivative and its corresponding radiolabeled immunoconjugates
AUTHOR(S): Li, Min; Meares, Claude F.
CORPORATE SOURCE: Dep. Chem., Univ. California, Davis, CA, 95616-0935, USA
SOURCE: Bioconjugate Chem. (1993), 4(4), 275-83
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English

AB By directly coupling a tetrapeptide to DOTA through an amide bond, a novel DOTA deriv., DOTA-glycylglycylglycyl-L-p-nitrophenylalanine amide, was synthesized. This new precursor bifunctional chelating agent was converted to DOTA-glycylglycylglycyl-L-p-isothiocyanatophenylalanine and conjugated to monoclonal antibody Lym-1. Serum stability studies show that the radiolabeled conjugates are kinetically inert under physiol.

conditions. The rates of loss of radiometals in human serum are 0.1% per day for In3+, 0.02% per day for Y3, and 0.3% per day for Cu2+-labeled immunoconjugates. In the presence of the liver enzyme cathepsin B, an in vitro digestion of 114mIn-labeled conjugate yields a small fragment contg. 114mIn. Characterization of the cleavage products shows that this liver enzyme hydrolyzes the peptide linkage before the phenylalanine residue, freeing the In-DOTA-triglycine complex from the conjugate. However, the liver enzyme cathepsin D does not cleave the linkage over the span of 7 days.

IT **149206-87-1DP**, radiometal-monoclonal antibody **conjugates**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and stability and enzyme digestion of)

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Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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5 RN **428817-79-2** REGISTRY

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35	RN	**277316-60-6**	REGISTRY
36	RN	**277316-56-0**	REGISTRY
37	RN	**277316-52-6**	REGISTRY
38	RN	**277316-45-7**	REGISTRY
39	RN	**277316-41-3**	REGISTRY
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65 RN **234442-93-4** REGISTRY
66 RN **234442-92-3** REGISTRY
67 RN **221328-05-8** REGISTRY
68 RN **213187-44-1** REGISTRY
69 RN **209277-09-8** REGISTRY
70 RN **204318-14-9** REGISTRY
71 RN **202932-51-2** REGISTRY
72 RN **193528-92-6** REGISTRY
73 RN **192221-19-5** REGISTRY
74 RN **192221-18-4** REGISTRY
75 RN **192221-17-3** REGISTRY
76 RN **177943-92-9** REGISTRY
77 RN **177943-91-8** REGISTRY
78 RN **177943-89-4** REGISTRY
79 RN **177943-88-3** REGISTRY
80 RN **175892-38-3** REGISTRY
81 RN **150467-20-2** REGISTRY
82 RN **149979-17-9** REGISTRY
83 RN **149206-88-2** REGISTRY
84 RN **149206-87-1** REGISTRY

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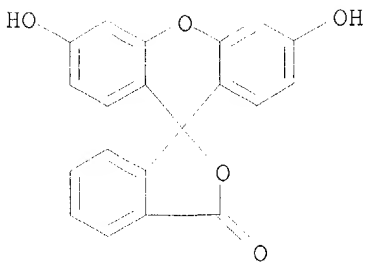
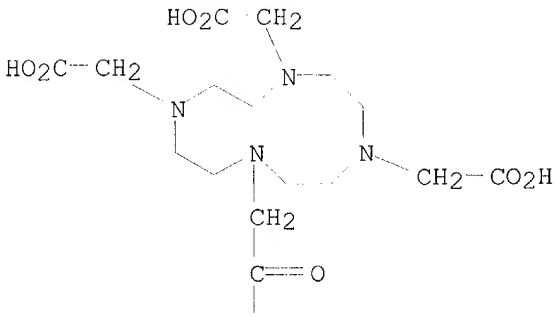
L12 ANSWER 1 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **436142-25-5** REGISTRY
CN INDEX NAME NOT YET ASSIGNED
MF C86 H114 N20 O22 S2
CI IDS
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 1-A





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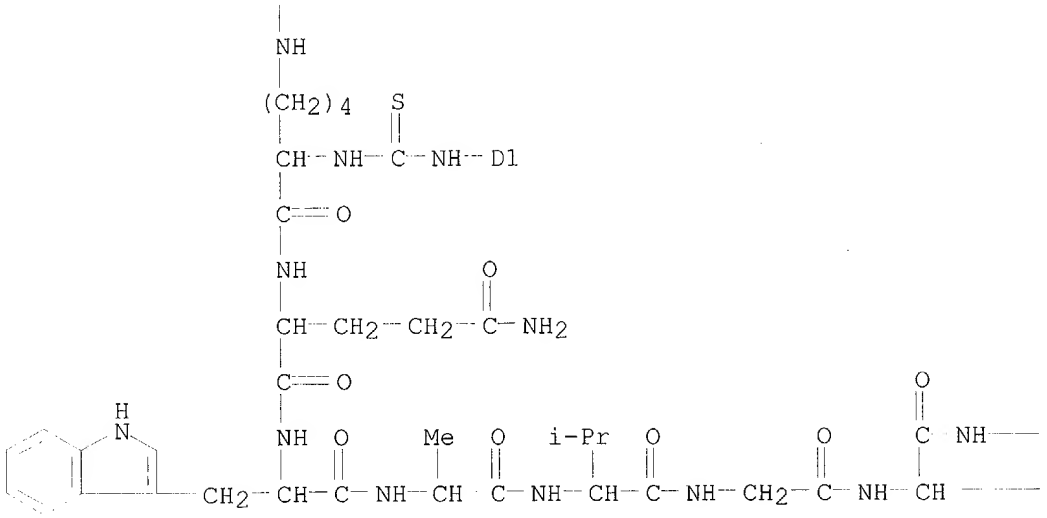
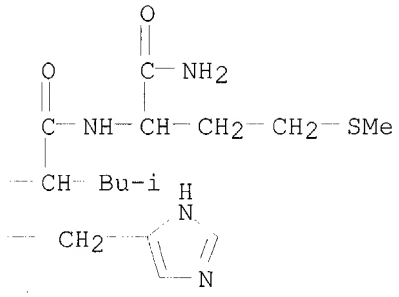




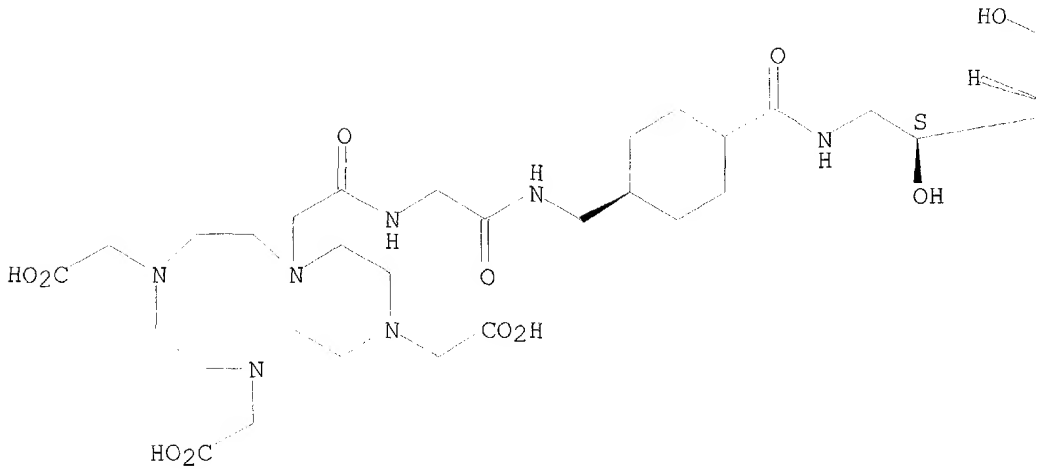
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 137:33520

L12 ANSWER 3 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **428817-81-6** REGISTRY
CN L-Ascorbic acid, 6-deoxy-6-[[[trans-4-[[[[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]acetyl]amino]methyl]cyclohexyl]carbonyl]amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H51 N7 O14
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



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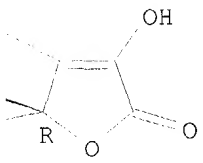


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

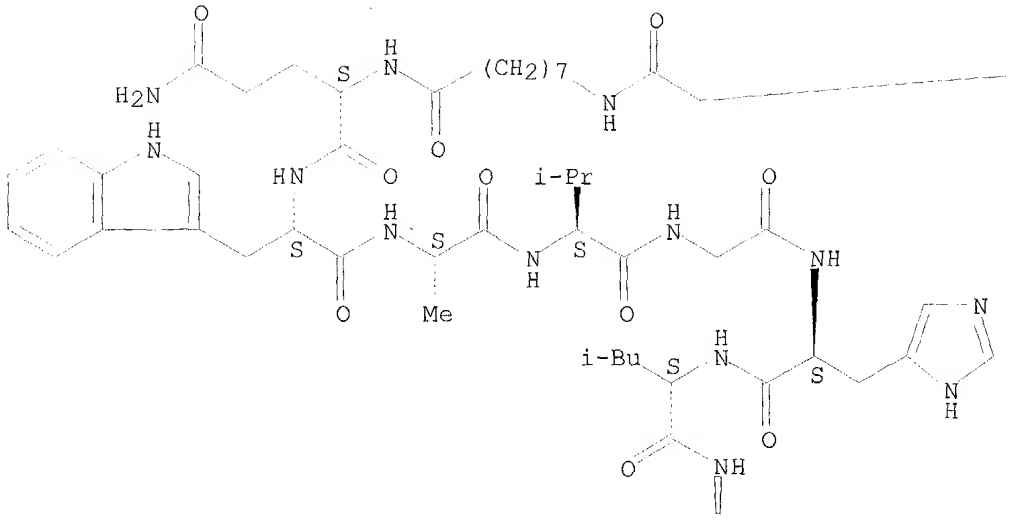
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:406944

L12 ANSWER 9 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **422512-81-0** REGISTRY
CN L-Methioninamide, N2-[1-oxo-8-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]octyl]-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C67 H106 N18 O17 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PAGE 1-A



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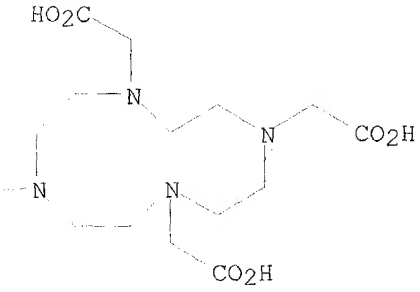

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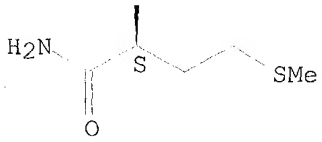

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:365879

L12 ANSWER 13 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **415697-94-8** REGISTRY
CN L-Phenylalanine, N2-[1-oxo-6-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]hexyl]-L-asparaginyl-L-seryl-L-seryl-L-asparaginyl-L-tyrosyl-L-cysteinyl-L-cysteinyl-L-.alpha.-glutamyl-L-leucyl-L-cysteinyl-L-cysteinyl-L-asparaginyl-L-prolyl-L-alanyl-L-cysteinyl-L-threonylglycyl-L-cysteinyl-, cyclic (6.fwdarw.11),(7.fwdarw.15),(10.fwdarw.18)-tris(disulfide) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C101 H149 N27 O37 S6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-B

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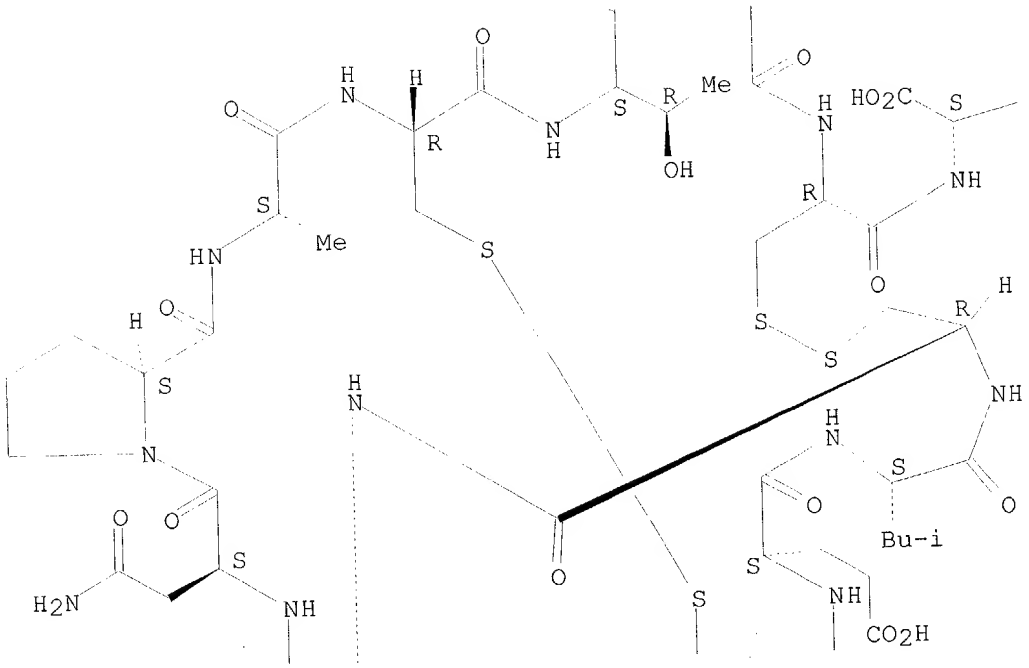

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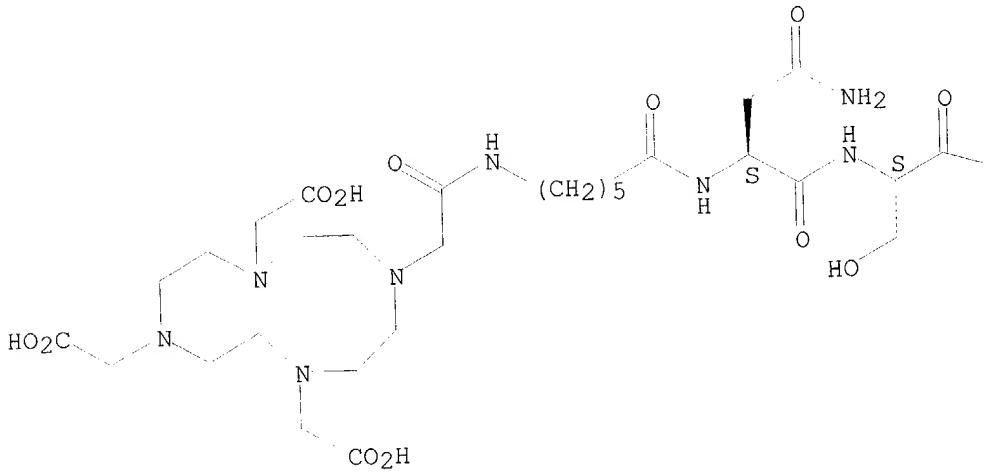
PAGE 3-A



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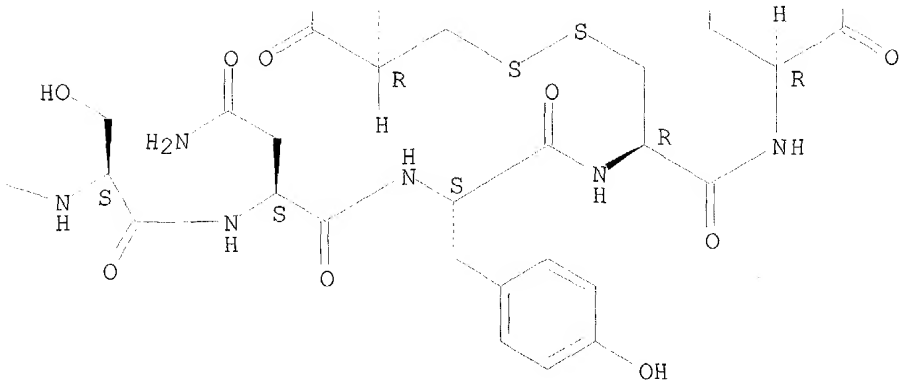


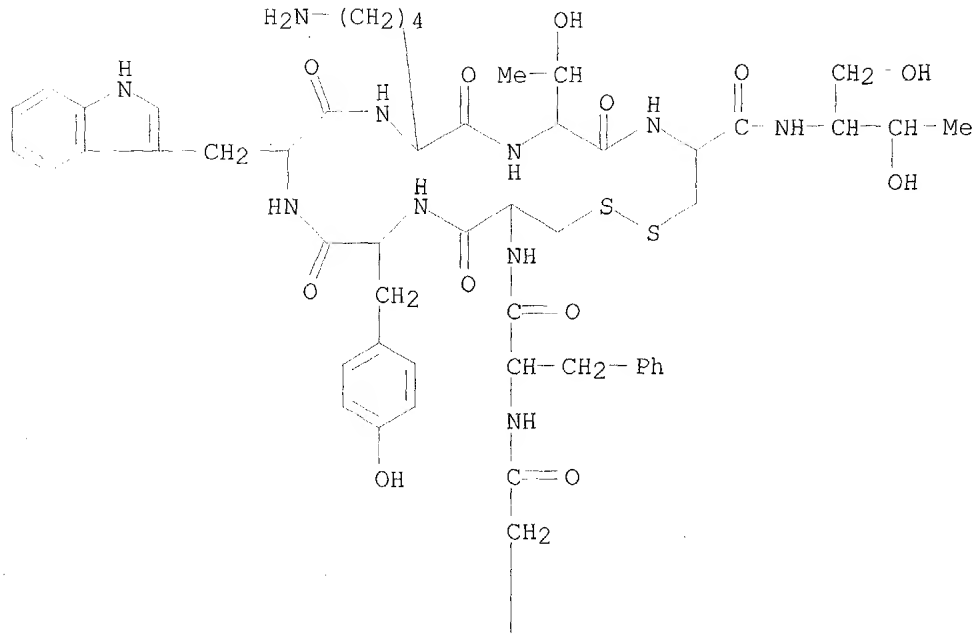
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

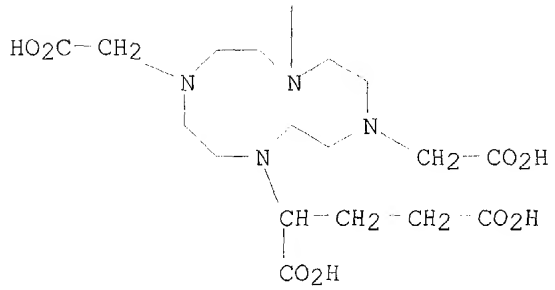
REFERENCE 1: 136:321356

L12 ANSWER 19 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **405263-92-5** REGISTRY
CN L-Cysteinamide, N-[[4,10-bis(carboxymethyl)-7-(1,3-dicarboxypropyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C68 H96 N14 O20 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 137:2480

REFERENCE 2: 136:272268

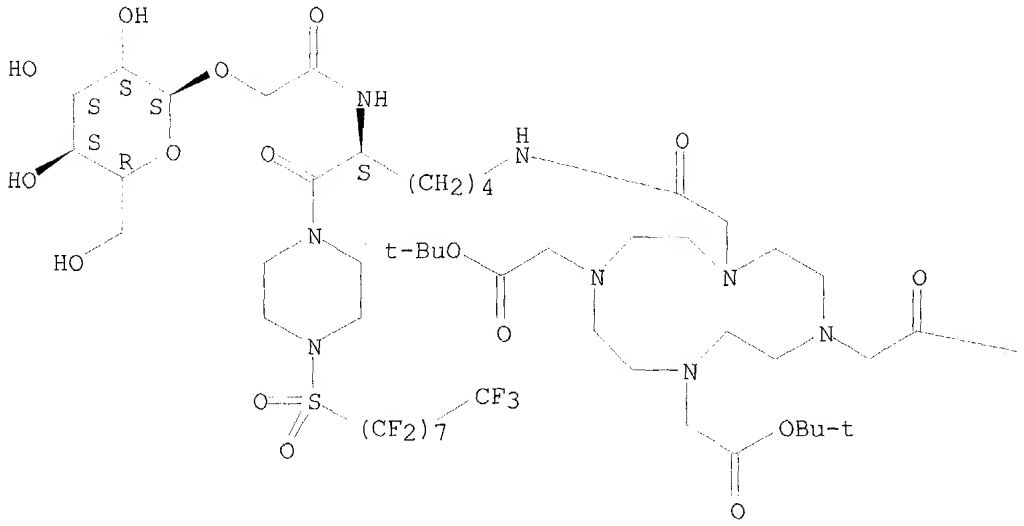
L12 ANSWER 20 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **400708-43-2** REGISTRY
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(5S)-6-[4-

[(heptadecafluorooctyl)sulfonyl]-1-piperazinyl]-5-[[(.alpha.-D-mannopyranosyloxy)acetyl]amino]-6-oxohexyl]amino]-2-oxoethyl]-, tris(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH
MF C54 H83 F17 N8 O17 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

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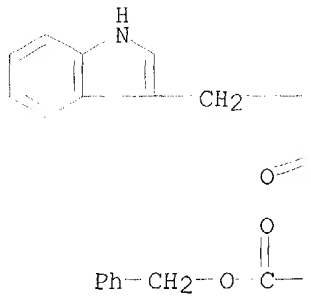
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:209641

REFERENCE 2: 136:209640

L12 ANSWER 21 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **387389-45-9** REGISTRY
CN L-Cysteine, N-[[4-(carboxymethoxy)phenyl][4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-alanylglycyl-L-cysteinyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-L-asparaginyl-L-phenylalanyl-L-phenylalanyl-L-tryptophyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-, cyclic (3.fwdarw.14)-disulfide, sodium salt (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C116 H148 N22 O33 S2 . x Na
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



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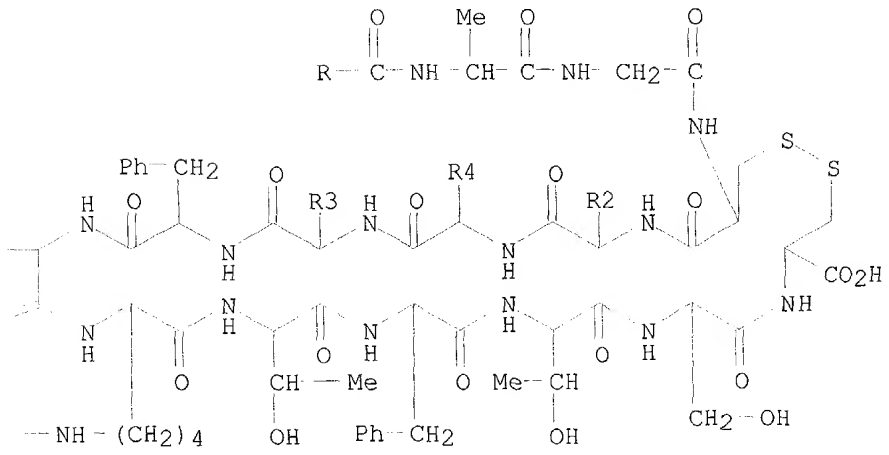
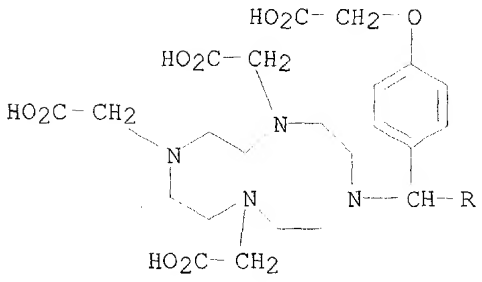
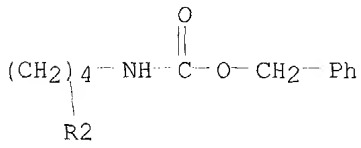


PAGE 2-A





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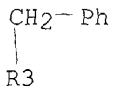

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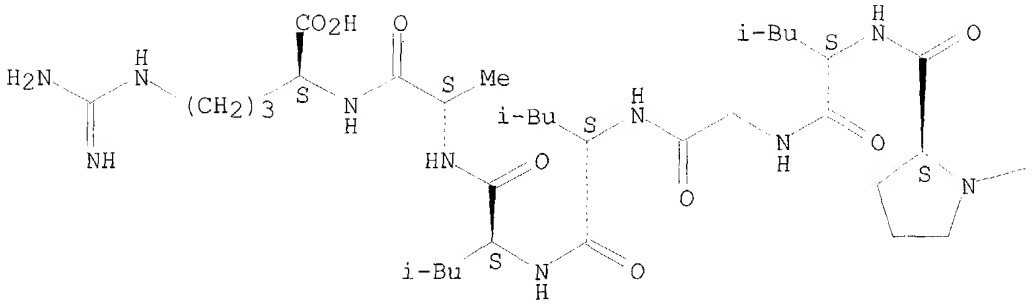
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:102654

L12 ANSWER 22 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **374804-69-0** REGISTRY
CN L-Arginine, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-cysteinylglycyl-L-prolyl-L-leucylglycyl-L-leucyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C55 H96 N16 O17 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



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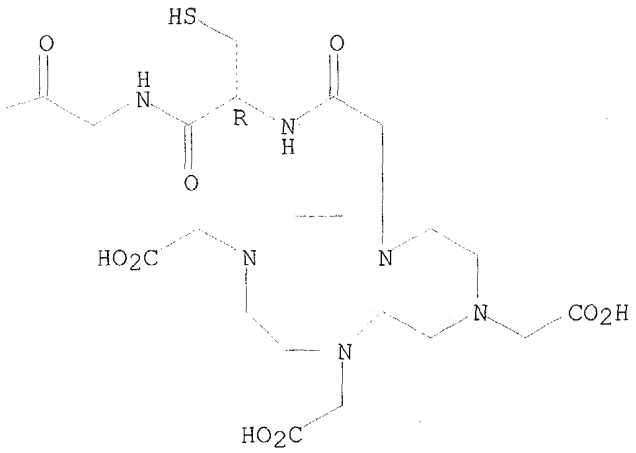


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

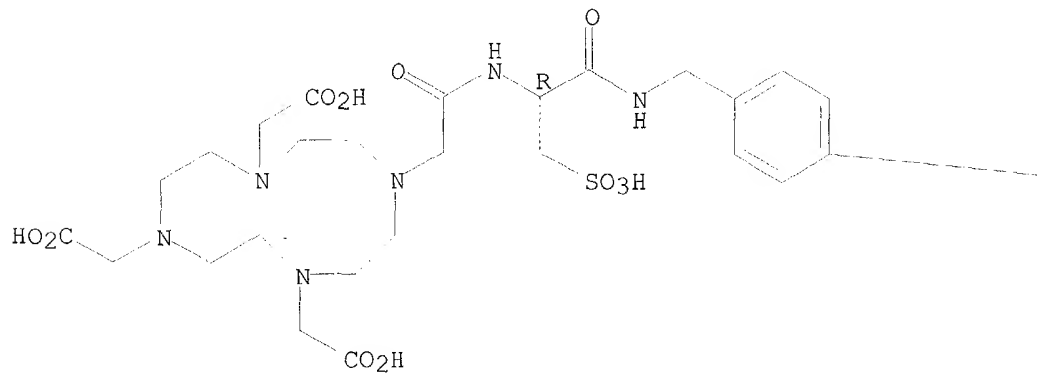
REFERENCE 1: 136:11092

L12 ANSWER 23 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **355149-97-2** REGISTRY
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(1R)-2-[[[4-[[[[(6S,7R,10S)-6-[(hydroxyamino)carbonyl]-7-(2-methylpropyl)-8-oxo-2-oxa-9-azabicyclo[10.2.2]hexadeca-12,14,15-trien-10-yl]carbonyl]amino]methyl]phenyl]methyl]amino]-2-oxo-1-(sulfomethyl)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C47 H69 N9 O16 S
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



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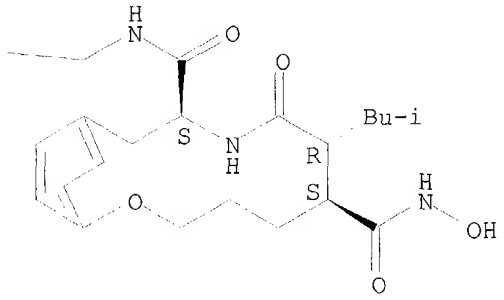


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:180952

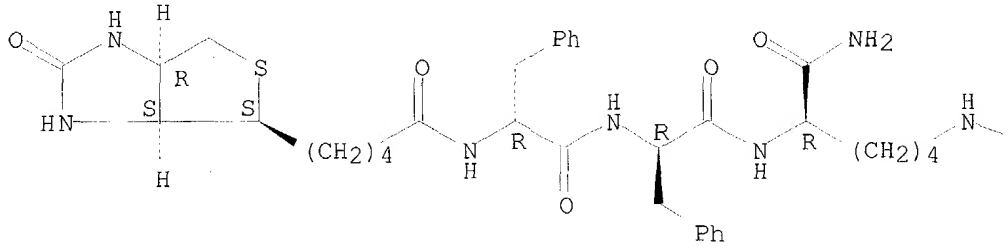
REFERENCE 2: 135:180950

L12 ANSWER 26 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **294637-28-8** REGISTRY
CN D-Lysinamide, N-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-D-phenylalanyl-D-phenylalanyl-N6-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH
MF C50 H73 N11 O12 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PAGE 1-A



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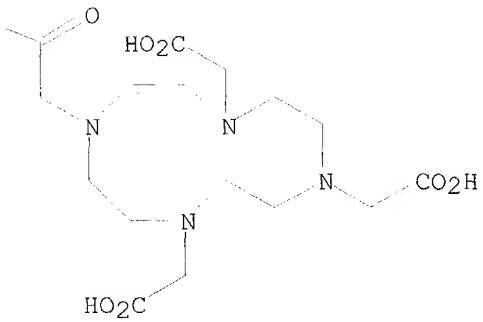


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

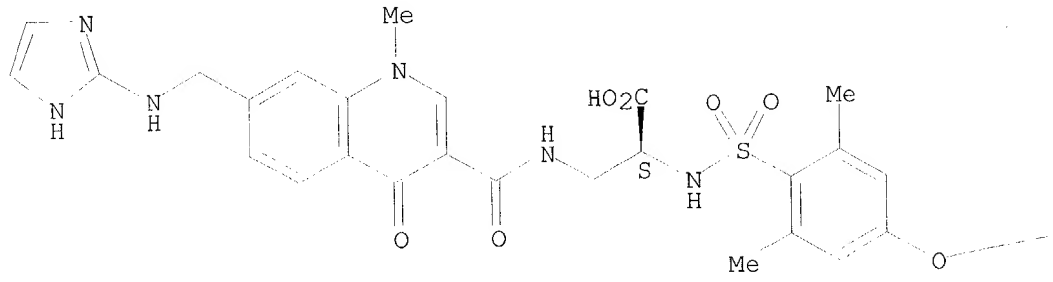
REFERENCE 1: 133:249059

L12 ANSWER 27 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **277316-68-4** REGISTRY
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[(4S)-4-[4-[[[bis(phosphonomethyl)amino]acetyl]amino]butyl]-24-[4-[[[(1S)-1-carboxy-2-[[[1,4-dihydro-7-[(1H-imidazol-2-ylamino)methyl]-1-methyl-4-oxo-3-quinolinyl]carbonyl]amino]ethyl]amino]sulfonyl]-3,5-dimethylphenoxy]-2,5,21-trioxo-10,13,16-trioxa-3,6,20-triazatetracos-1-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C66 H103 N15 O26 P2 S

SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



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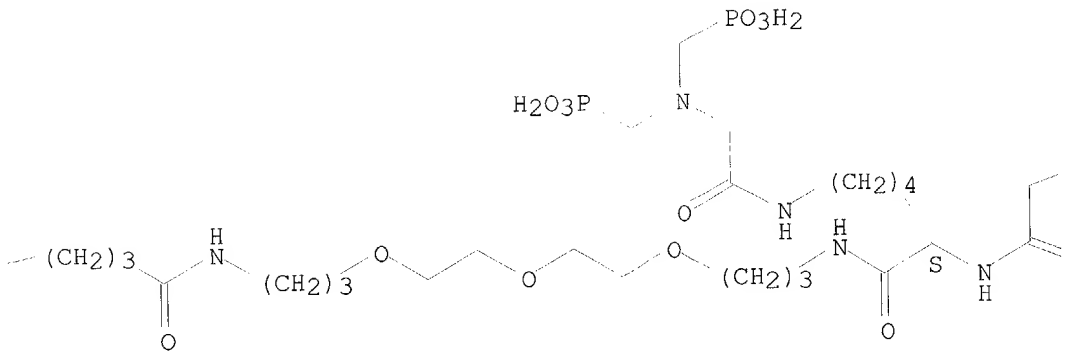

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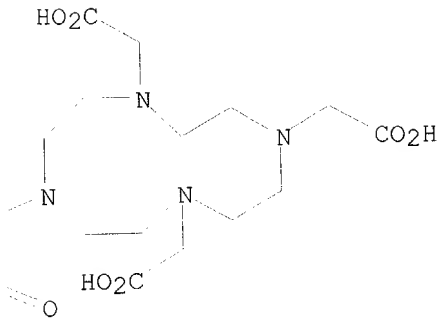


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:70082

REFERENCE 2: 133:59099

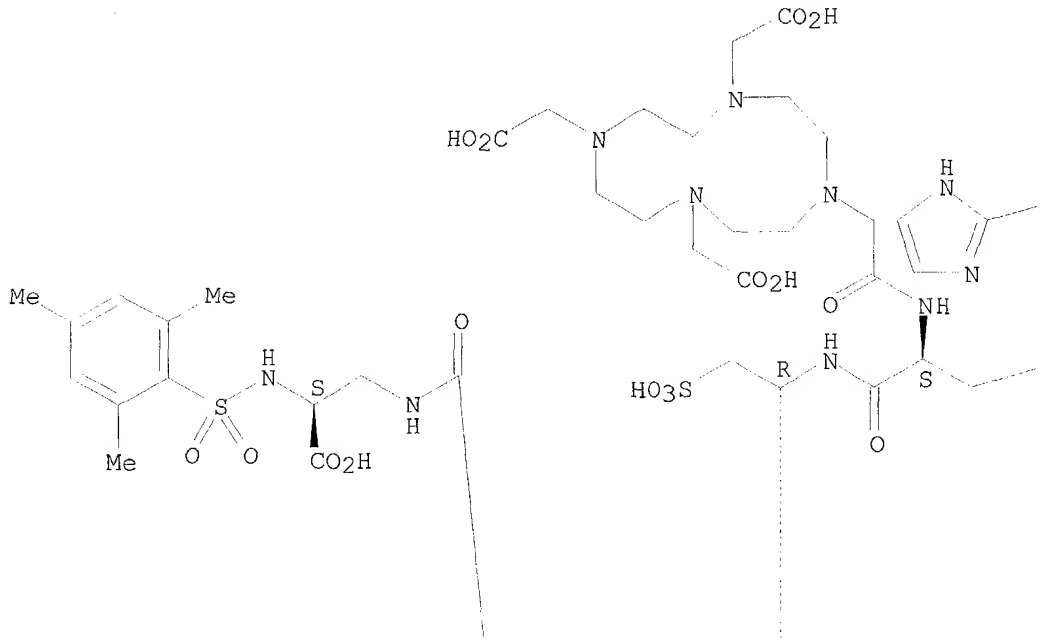
L12 ANSWER 43 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **277315-80-7** REGISTRY
CN L-Alaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoylbis[N-[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]-3-sulfo-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C85 H111 N21 O29 S4 . 2 C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 277315-79-4
CMF C85 H111 N21 O29 S4

Absolute stereochemistry.

PAGE 1-A



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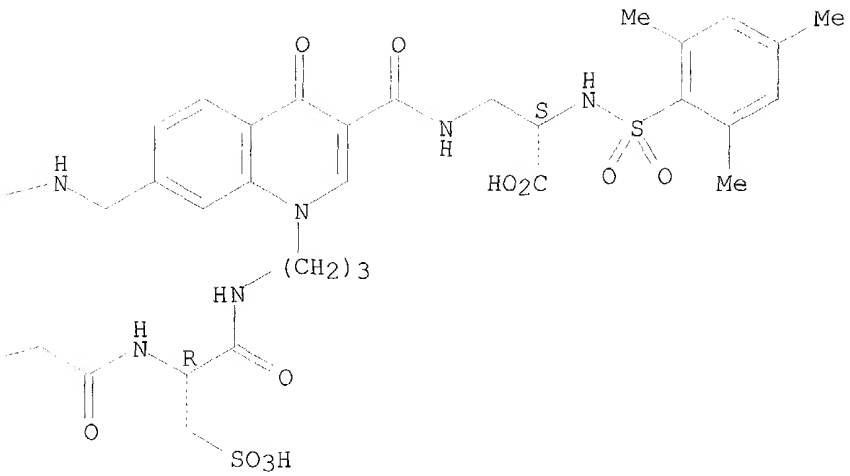

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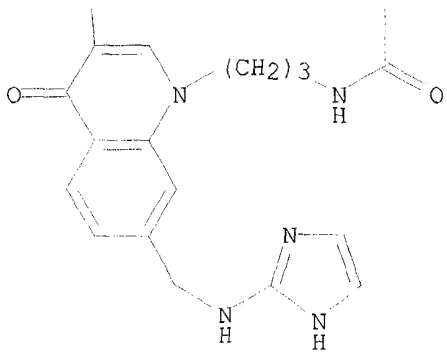
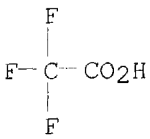


CM 2

CRN 76-05-1
CMF C2 H F3 O2



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

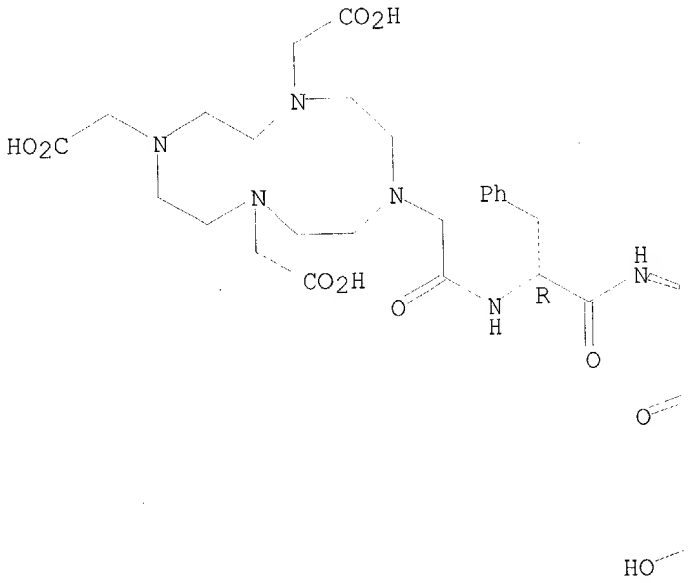
REFERENCE 1: 136:70082

REFERENCE 2: 133:59099

L12 ANSWER 54 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **251553-64-7** REGISTRY
CN L-Tryptophanamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C73 H96 N16 O16 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



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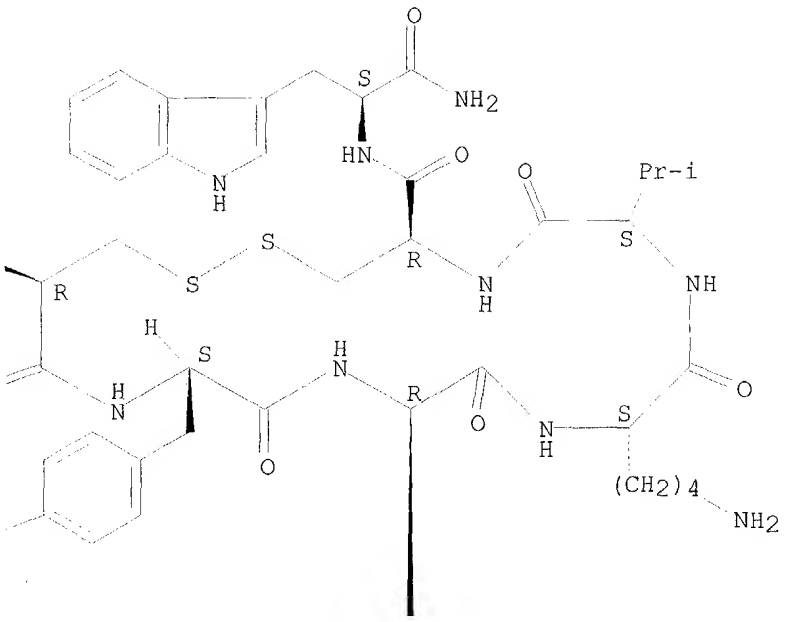

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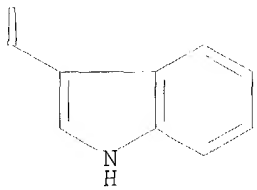


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:234514

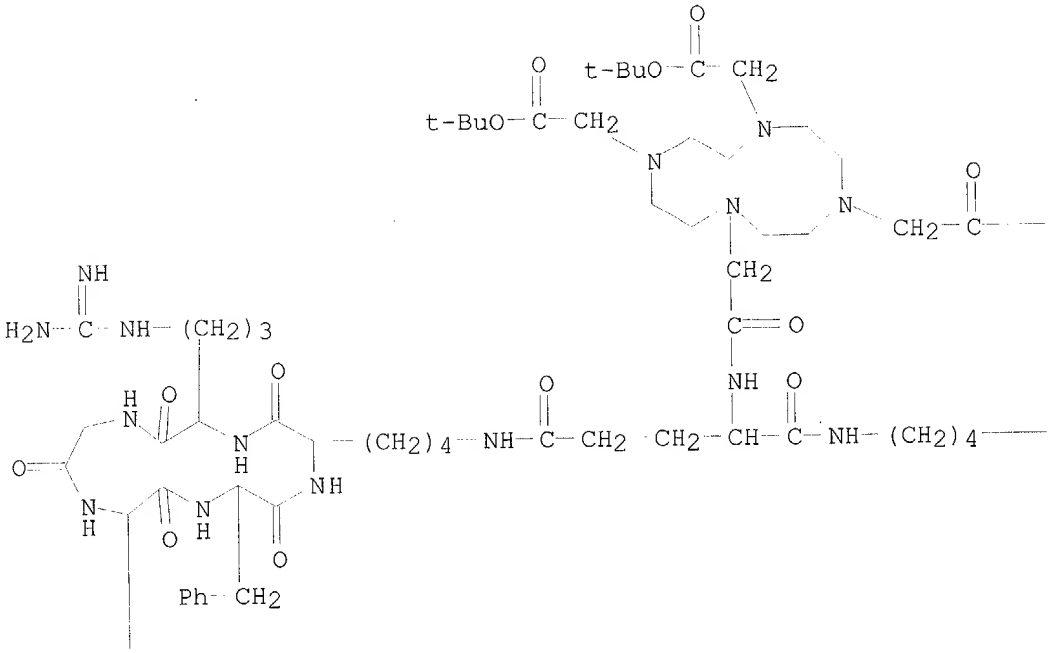
REFERENCE 2: 132:9203

L12 ANSWER 55 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **250612-82-9** REGISTRY
CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C87 H137 N23 O23 . 2 C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

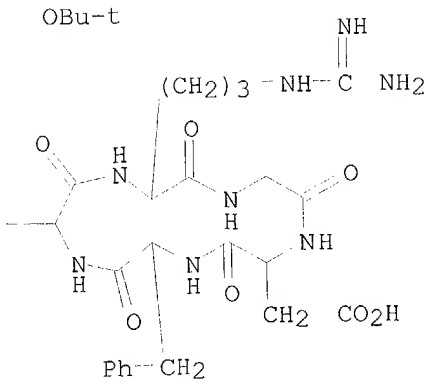
CM 1

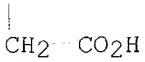
CRN 250612-81-8
CMF C87 H137 N23 O23

PAGE 1-A



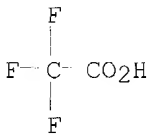
PAGE 1-B





CM 2

CRN 76-05-1
CMF C2 H F3 O2



3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:123597

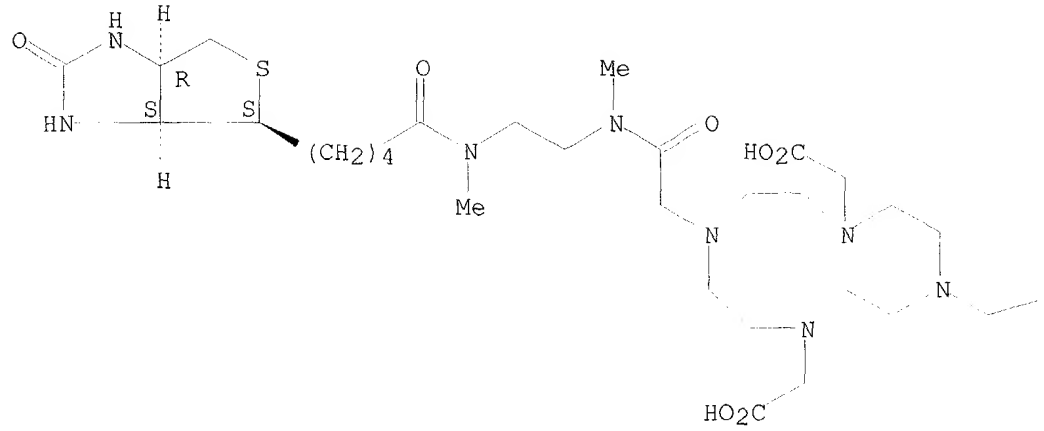
REFERENCE 2: 136:70083

REFERENCE 3: 131:351678

L12 ANSWER 59 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **245758-39-8** REGISTRY
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]methylamino]ethyl]methylamino]-2-oxoethyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H52 N8 O9 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

CO_2H

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

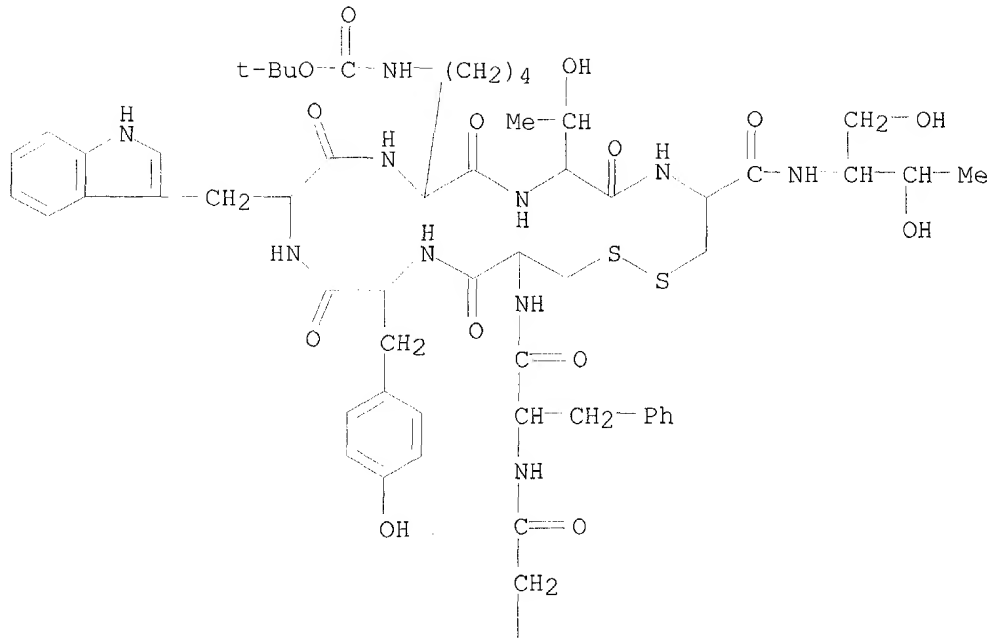
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:249059

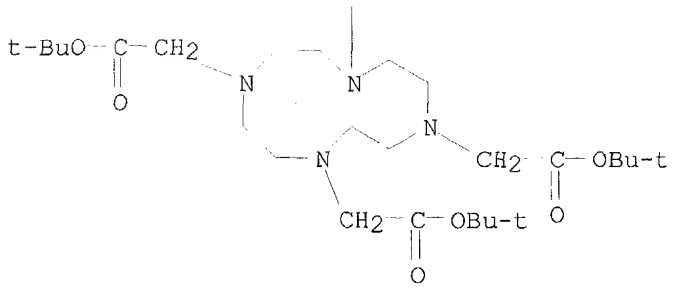
REFERENCE 2: 131:276952

L12 ANSWER 60 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **244219-77-0** REGISTRY
CN L-Cysteinamide, N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C82 H124 N14 O20 S2
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



PAGE 2-A



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

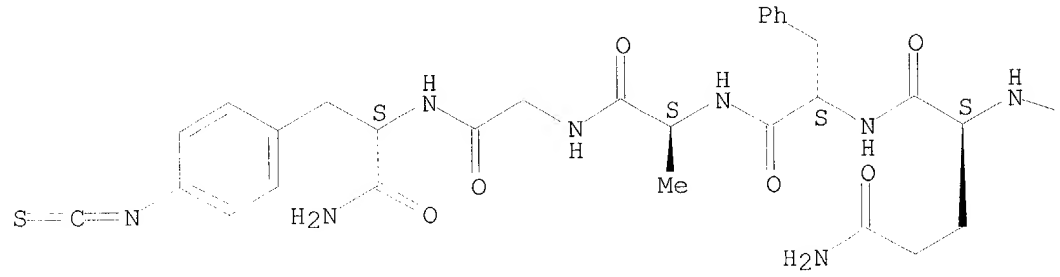
REFERENCE 1: 131:239827

L12 ANSWER 61 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **234442-97-8** REGISTRY
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycyl-L-phenylalanyl-L-glutaminylglycyl-L-valyl-L-glutaminyl-L-phenylalanyl-L-alanylglycyl-4-isothiocyanato- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C68 H94 N18 O19 S
SR CA

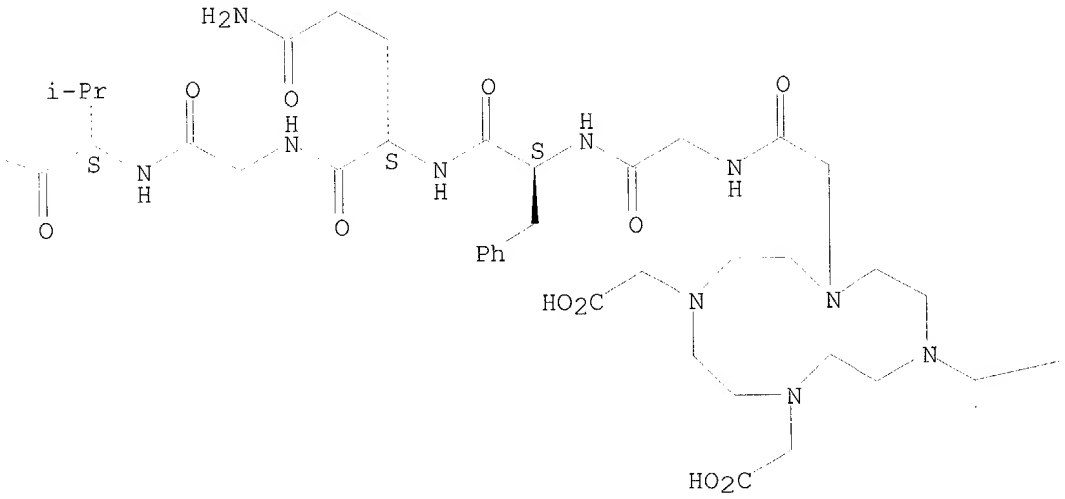
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 1-C

CO_2H

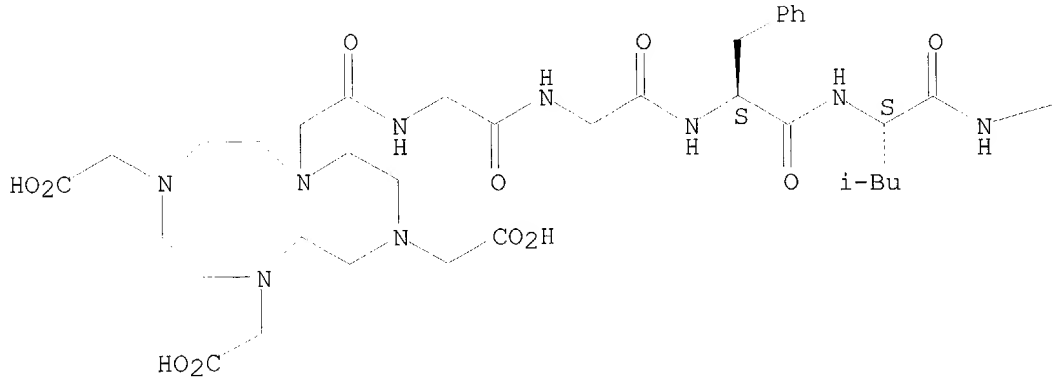
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:127216

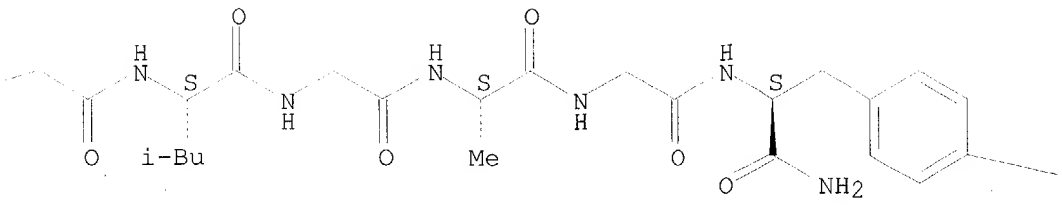
L12 ANSWER 67 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **221328-05-8** REGISTRY
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycyl-L-phenylalanyl-L-leucylglycyl-L-leucylglycyl-L-alanylglycyl-4-nitro- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C59 H88 N16 O19
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 1-C

NO_2

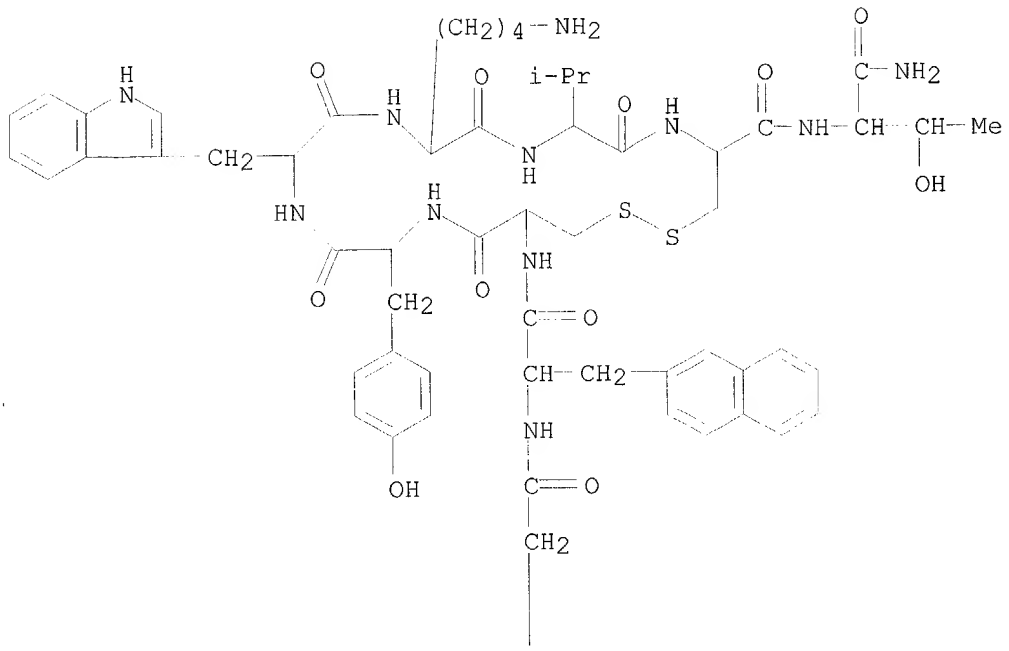
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:127216

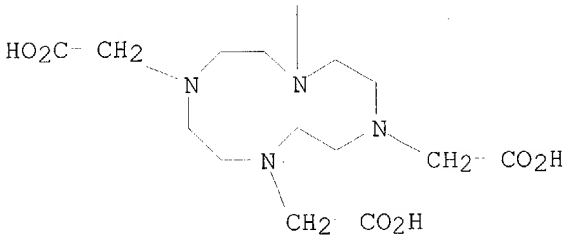
REFERENCE 2: 130:237860

L12 ANSWER 68 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **213187-44-1** REGISTRY
CN L-Threoninamide, 3-(2-naphthalenyl)-N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C70 H95 N15 O17 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 1-A



PAGE 2-A



3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:234514

REFERENCE 2: 132:9203

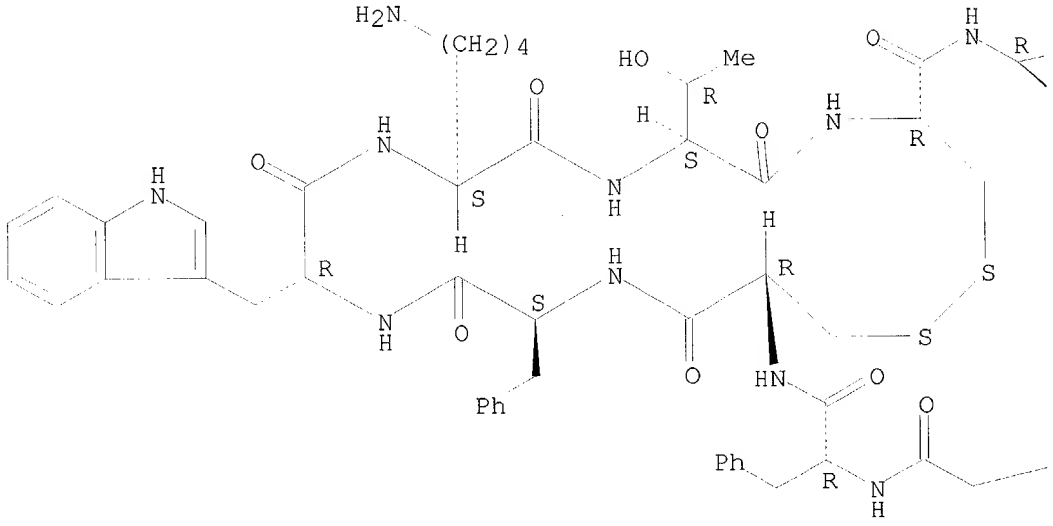
REFERENCE 3: 129:245497

L12 ANSWER 69 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **209277-09-8** REGISTRY
CN L-Cysteinamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH

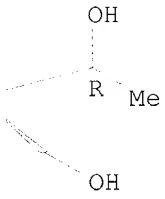
MF C65 H92 N14 O17 S2
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

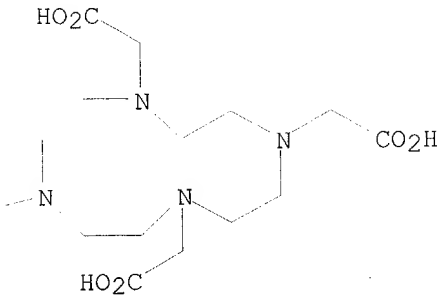
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B





7 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:234514

REFERENCE 2: 132:3542

REFERENCE 3: 131:113202

REFERENCE 4: 131:32155

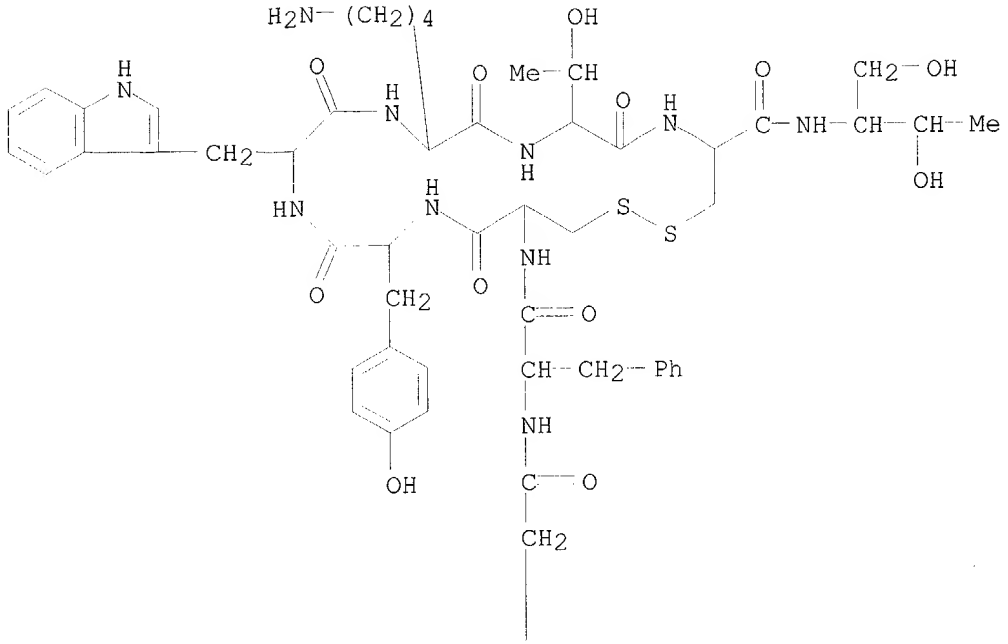
REFERENCE 5: 130:223601

REFERENCE 6: 129:257023

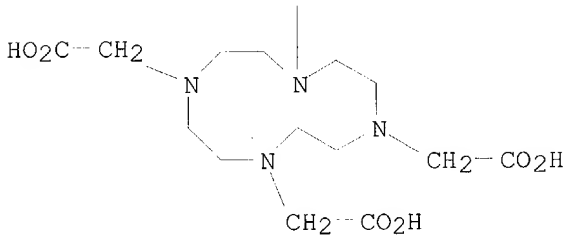
REFERENCE 7: 129:81945

L12 ANSWER 70 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **204318-14-9** REGISTRY
CN L-Cysteinamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (DOTA-D-Phe1,Tyr3)octreotide
CN DOTATOC
CN Edotreotide
CN SDZ-SMT 487
CN SMT 487
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C65 H92 N14 O18 S2
CI COM
SR CA
LC STN Files: CA, CAPLUS, PHAR, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 2-A



12 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
12 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:275446

REFERENCE 2: 136:272268

REFERENCE 3: 136:196247

REFERENCE 4: 135:149232

REFERENCE 5: 134:152628

REFERENCE 6: 134:127855

REFERENCE 7: 134:2116

REFERENCE 8: 133:234514

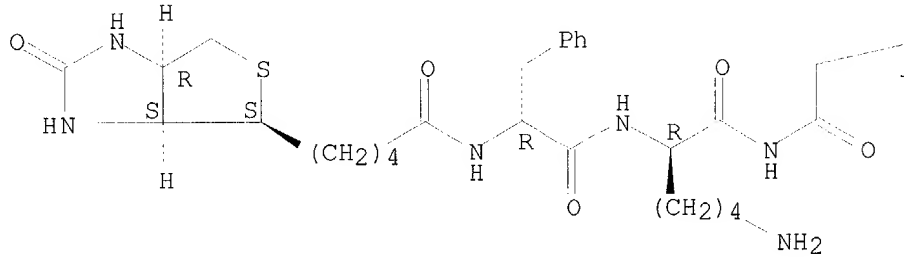
REFERENCE 9: 132:9203

REFERENCE 10: 131:239827

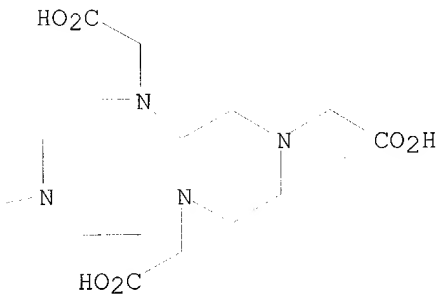
L12 ANSWER 71 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **202932-51-2** REGISTRY
CN D-Lysinamide, N-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-D-phenylalanyl-N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C41 H64 N10 O11 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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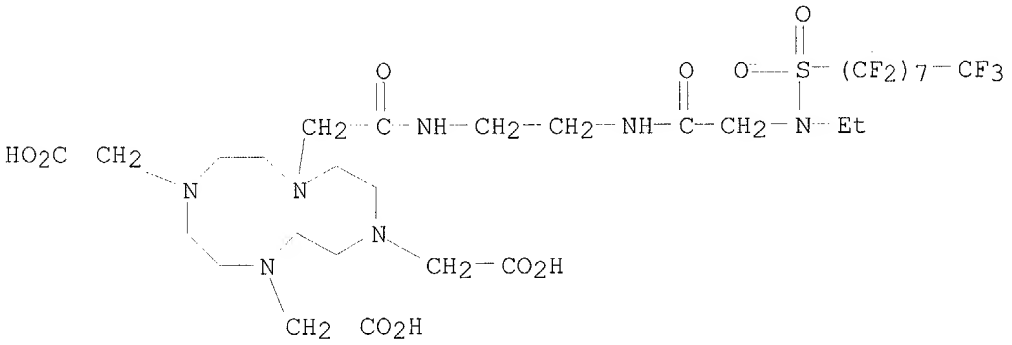
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:172129

L12 ANSWER 72 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **193528-92-6** REGISTRY
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(9-ethyl-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluoro-10,10-dioxido-2,7-dioxo-10-thia-3,6,9-triazaoctadec-1-yl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C30 H40 F17 N7 O10 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

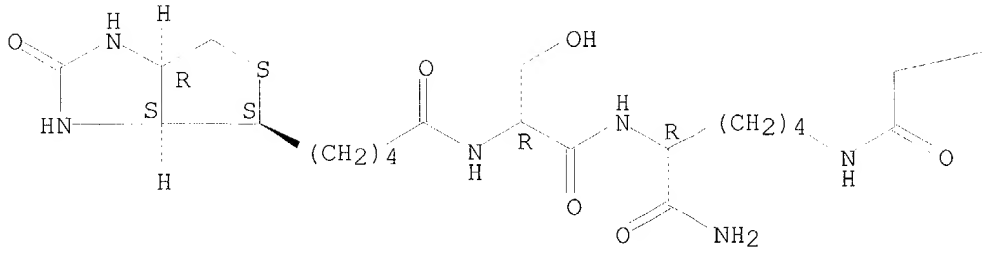
REFERENCE 1: 127:228839

REFERENCE 2: 127:170662

L12 ANSWER 73 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **192221-19-5** REGISTRY
CN D-Lysinamide, N-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-D-seryl-N6-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H60 N10 O12 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PAGE 1-A



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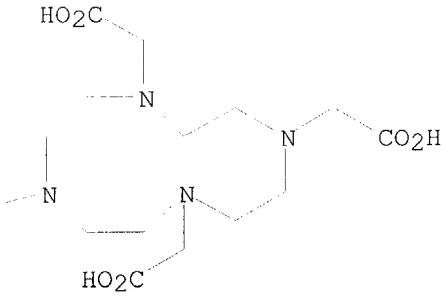


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:249059

REFERENCE 2: 127:92211

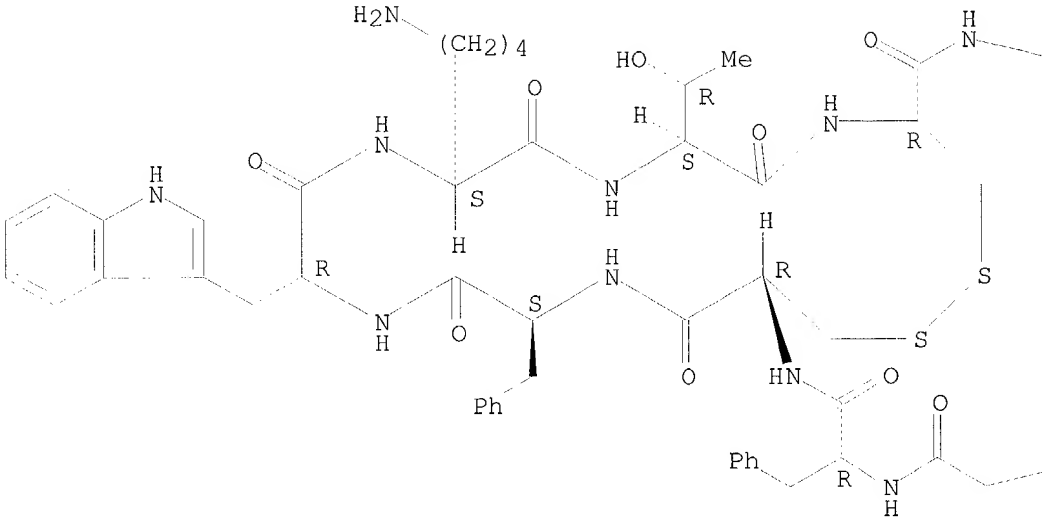
L12 ANSWER 76 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **177943-92-9** REGISTRY
CN L-Threonine, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide, acetate (salt) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C65 H90 N14 O18 S2 . x C2 H4 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CM 1

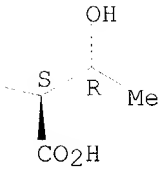
CRN 177943-91-8
CMF C65 H90 N14 O18 S2

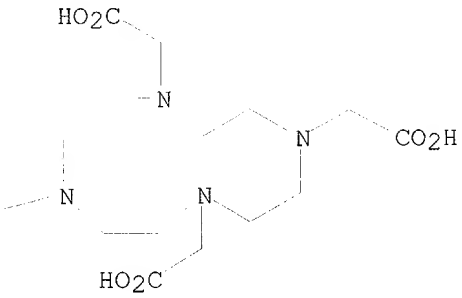
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B





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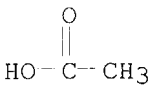


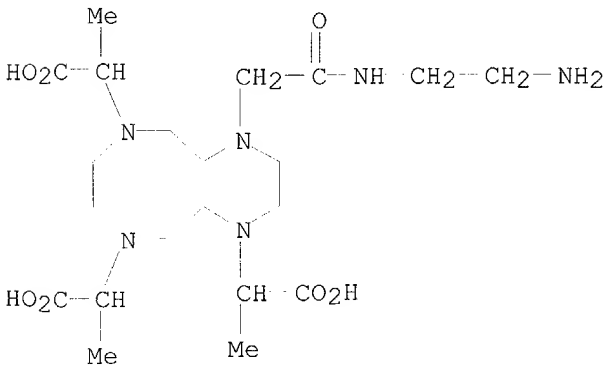
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:59133

L12 ANSWER 80 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **175892-38-3** REGISTRY
CN Chitosan, 2-hydroxyethyl ether, polymer with 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-.alpha.,.alpha.',.alpha.''-trimethyl-1,4,7,10-tetraazacyclododecane-1,4,7-tricarboxylic acid (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-tricarboxylic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-.alpha.,.alpha.',.alpha.''-trimethyl-, polymer with chitosan 2-hydroxyethyl ether (9CI)
MF (C21 H40 N6 O7 . C2 H6 O2 . x Unspecified)x
CI PMS
PCT Manual component, Polyamide, Polyamide formed, Polyamine, Polyester, Polyester formed
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 149979-17-9
CMF C21 H40 N6 O7



CM 2

CRN 39280-86-9
CMF C2 H6 O2 . x Unspecified

CM 3

CRN 9012-76-4
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

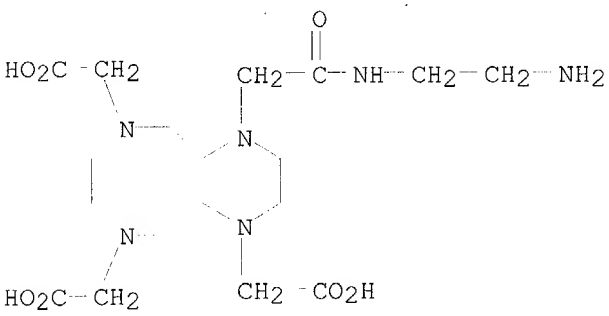
CRN 107-21-1
CMF C2 H6 O2

HO-CH2-CH2-OH

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:311363

L12 ANSWER 81 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **150467-20-2** REGISTRY
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H34 N6 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

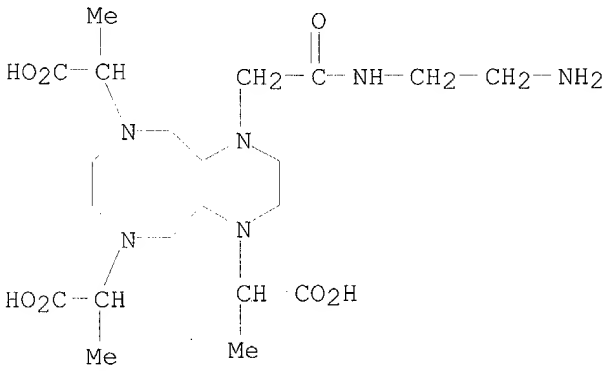
REFERENCE 1: 125:80777

REFERENCE 2: 124:139993

REFERENCE 3: 122:75613

REFERENCE 4: 119:220702

L12 ANSWER 82 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **149979-17-9** REGISTRY
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-tricarboxylic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-.alpha.,.alpha.',.alpha.''-trimethyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN DO 3MA
FS 3D CONCORD
MF C21 H40 N6 O7
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:29269

REFERENCE 2: 124:311363

REFERENCE 3: 124:283286

REFERENCE 4: 120:164250

REFERENCE 5: 119:176732

L12 ANSWER 84 OF 84 REGISTRY COPYRIGHT 2002 ACS
RN **149206-87-1** REGISTRY
CN L-Phenylalanine, 4-isothiocyanato-N-[N-[N-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycyl]glycyl]glycyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,4,7,10-Tetraazacyclododecane, L-phenylalanine deriv.
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C32 H45 N9 O12 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

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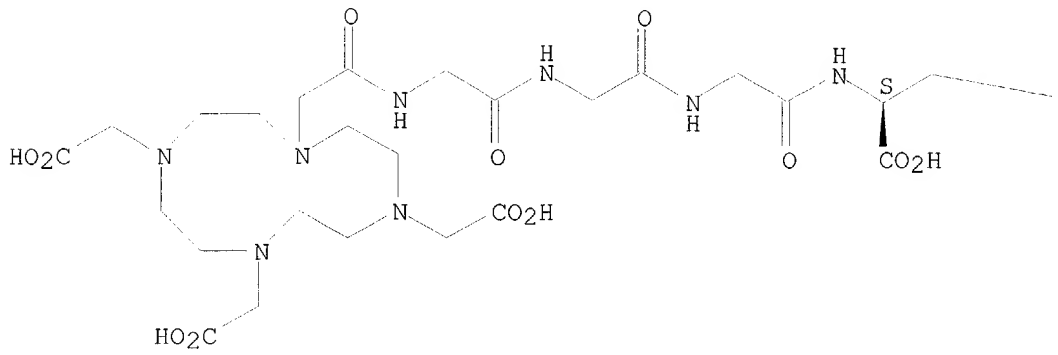
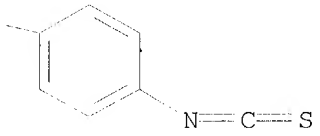


PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:90207